AcuFocus KAMRA™ Inlay

United States Food and Drug Administration
Ophthalmic Devices Advisory Committee
June 6, 2014

AcuFocus

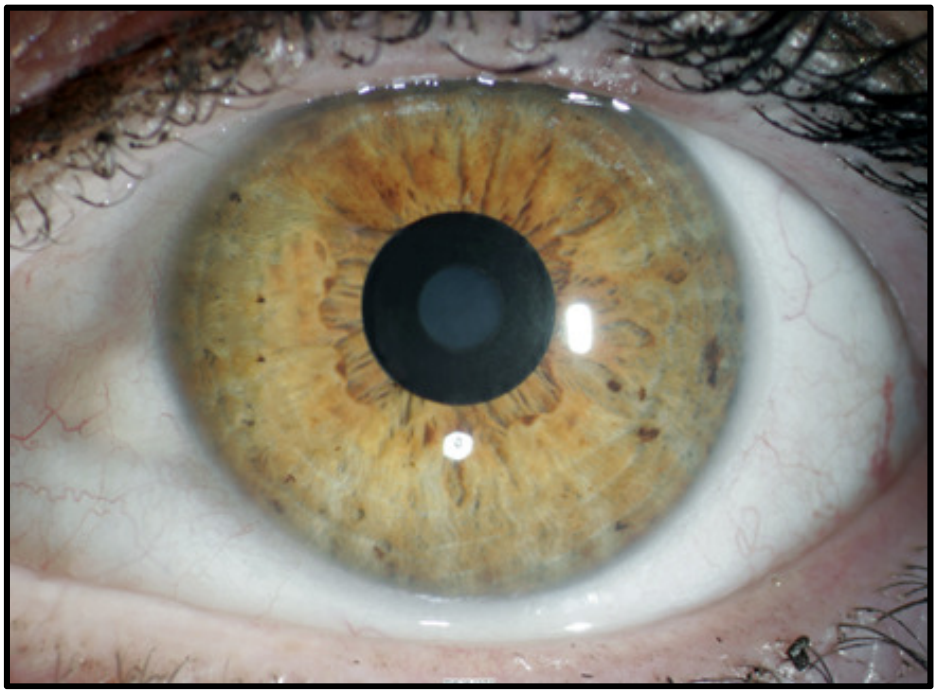
Introduction

Nicholas Tarantino, O.D.
Chief Clinical and Regulatory Officer
AcuFocus, Inc.

KAMRA Inlay – Proposed Indication

- **The KAMRA™ Inlay is indicated for the improvement of near vision in presbyopic patients who require near correction. The inlay is intended to be placed intrastromally in the cornea, on the visual axis, by way of a femtosecond laser-created pocket using a spot/line separation of 6×6 microns or less. The inlay should be placed at a depth equal to or greater than 180 µm.**

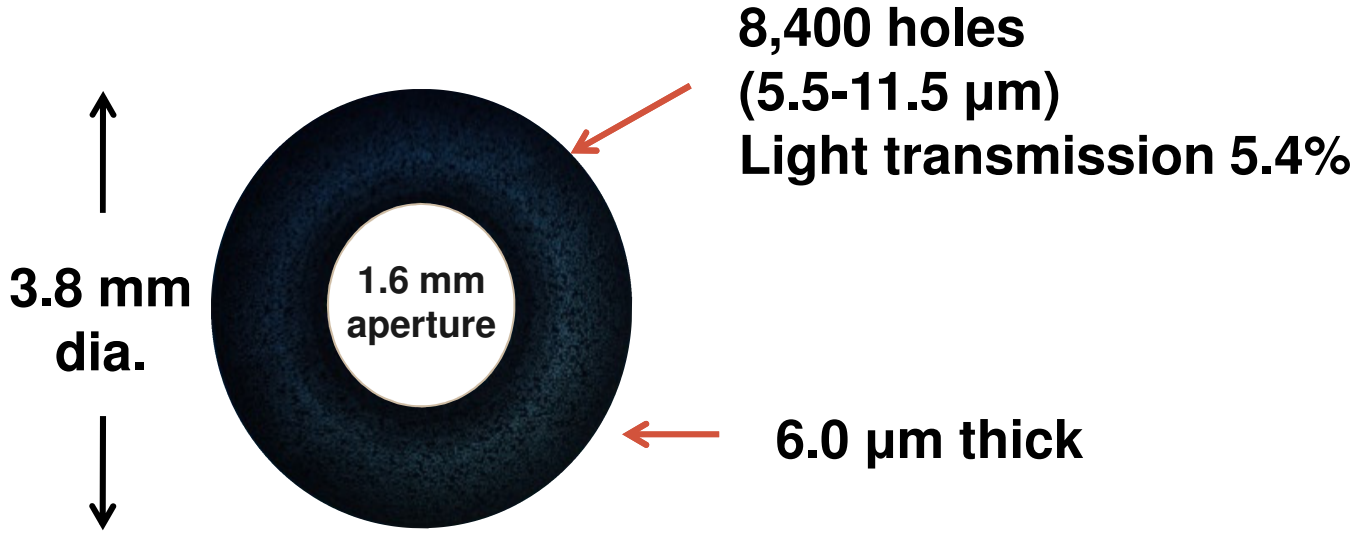
KAMRA Inlay



- The inlay has no refractive power
- Small, central aperture expands depth of focus, thus improving near vision

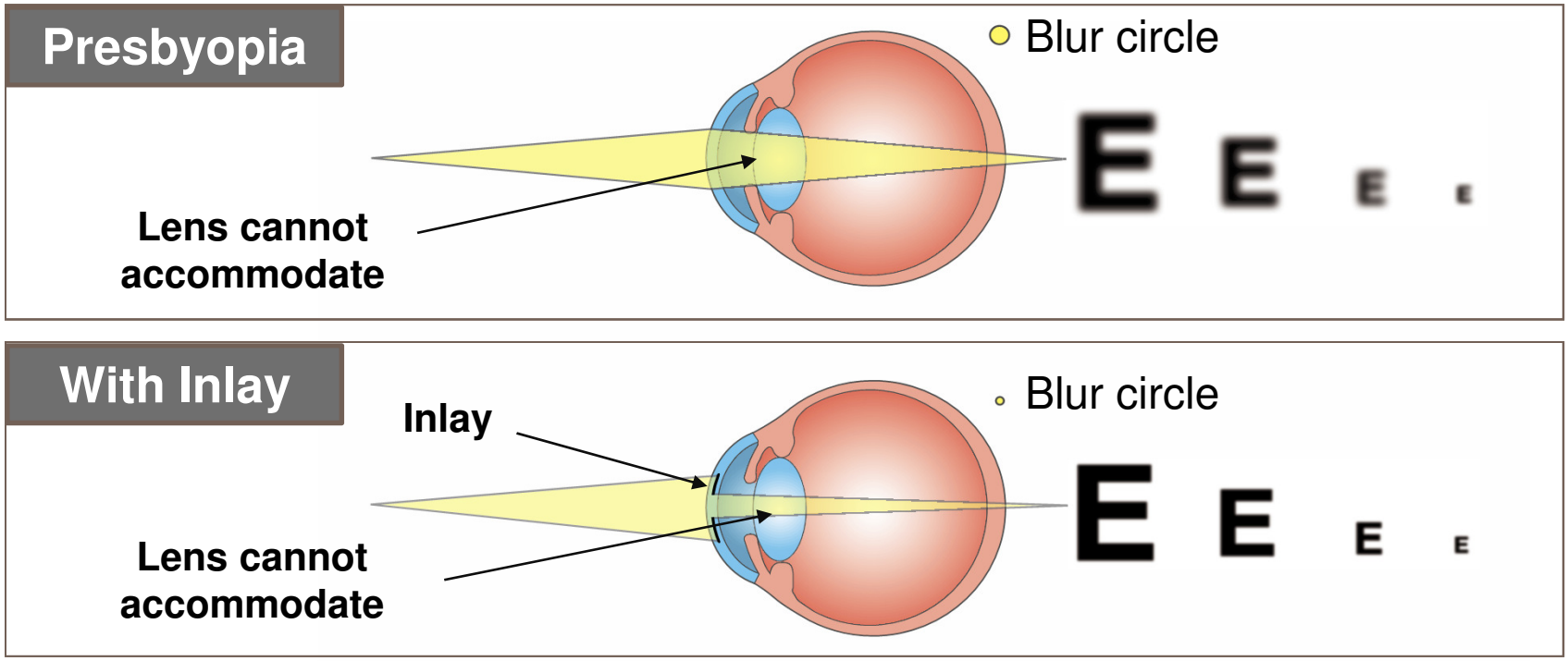
KAMRA Inlay – Key Design Features

- **Hole pattern optimized for safety and effectiveness**
  - **Maximize nutrient flow and minimize visual symptoms**



Profile view
7.5 mm posterior radius of curvature

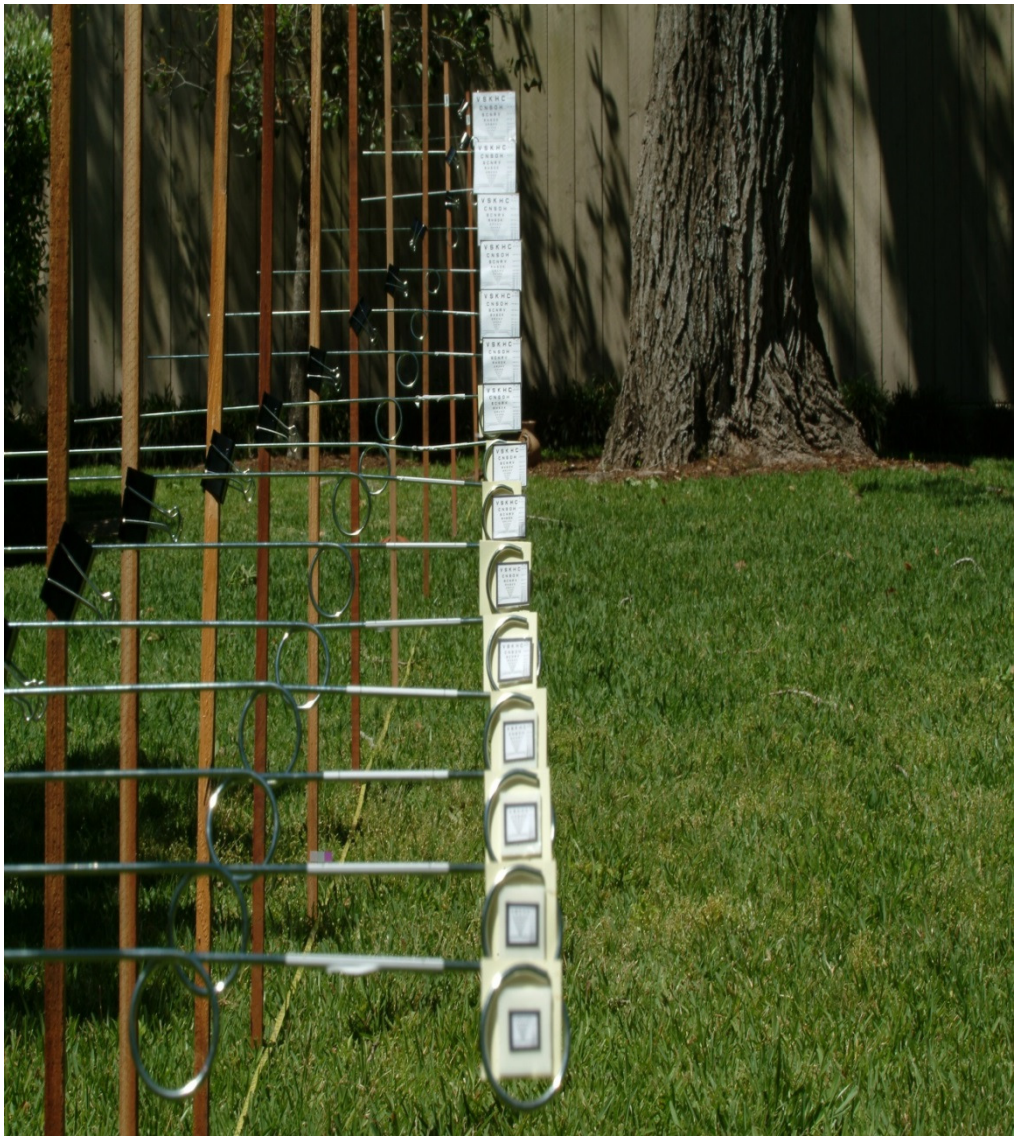
Extending the Depth of Focus



Demonstration of Concept of Depth of Focus (Moderate Aperture)

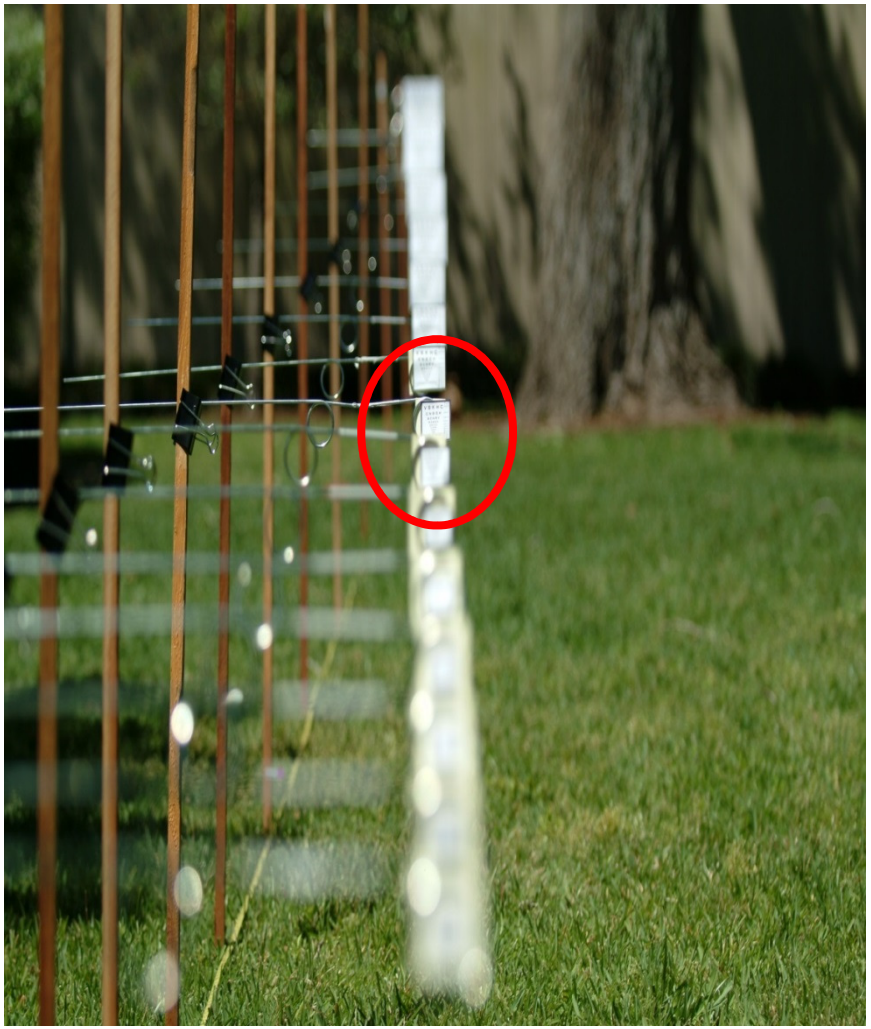
- Simulation of vision with ~4.0 mm pupil using an SLR camera
- (2 legible targets)

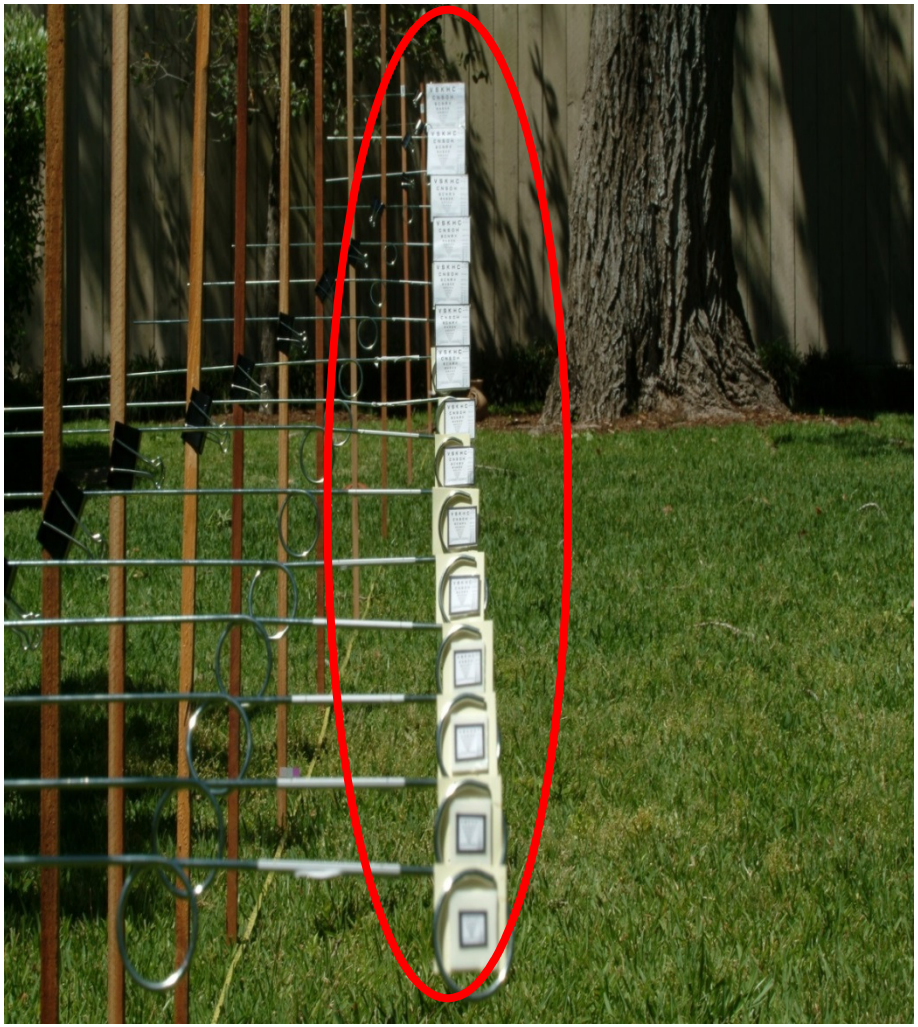
Demonstration of Concept of Depth of Focus (Small Aperture)



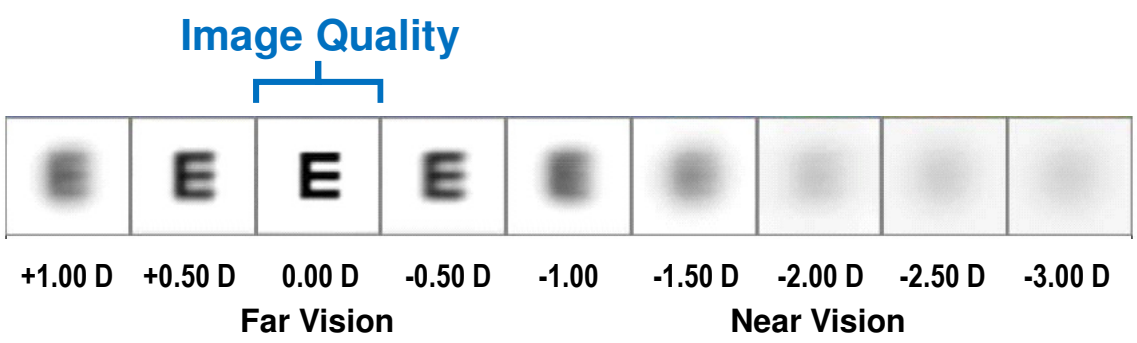
- Simulation of vision with ~1.6 mm pupil using an SLR camera
- (13 legible targets)

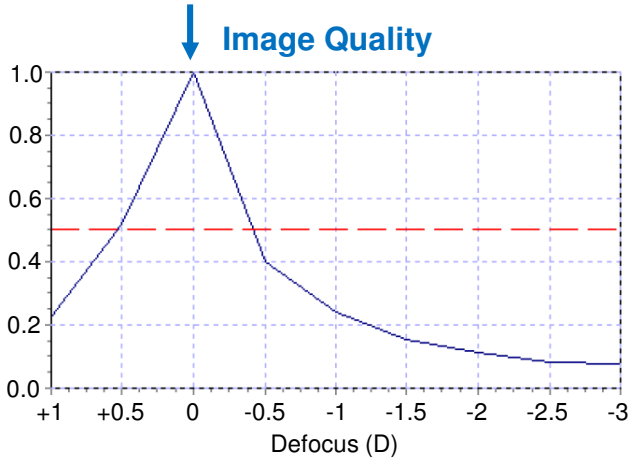
Simulation of Extended Depth of Focus



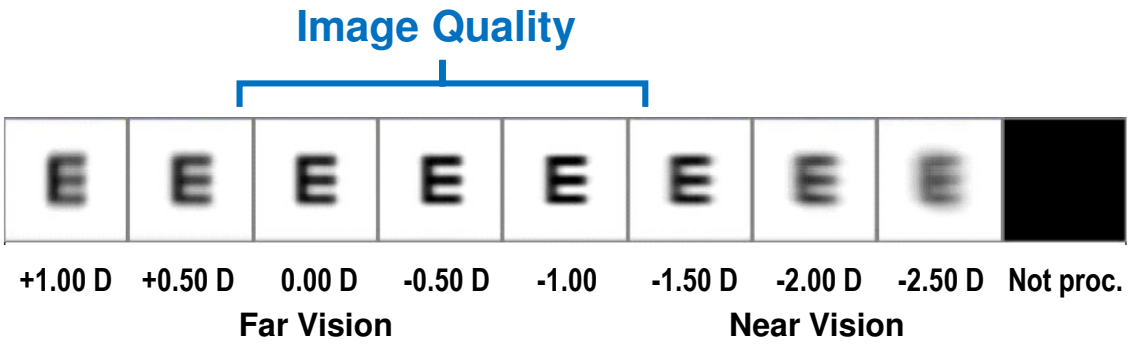


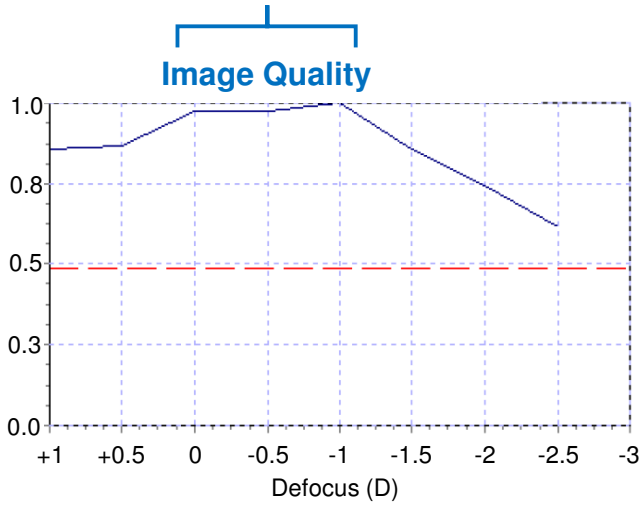
Defocus Curves





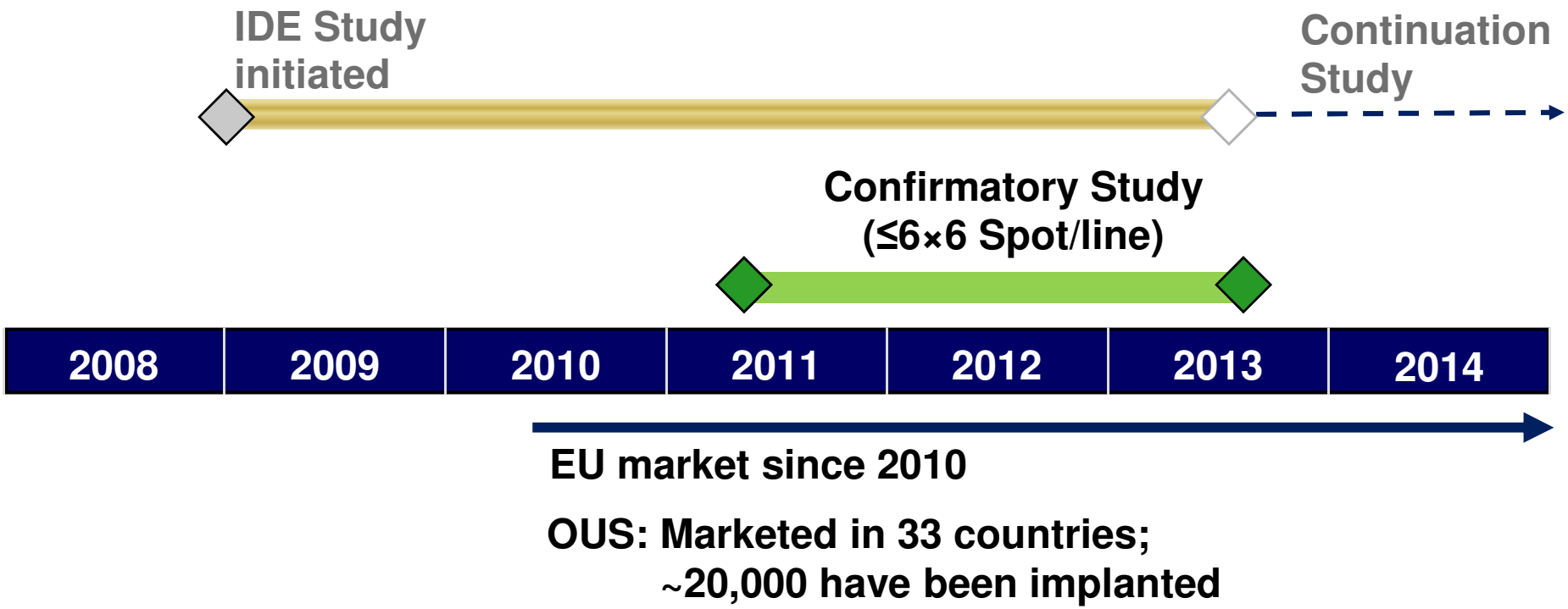
Non-implanted Presbyopic Eye





KAMRA Eye

Regulatory History



OUS: Marketed in 33 countries;
~20,000 have been implanted

Post-Marketing Study

- We have initiated a continuation study protocol to extend study follow-up out to 5 years
- A post-approval study will be implemented to monitor any AE and to follow long-term vision stability

Global Registry

- A global data registry for monitoring and supervision was established in February 2013
- https://acufocus.acceleratedvision.com/OAS/login/preLogin.do

Information not reviewed by FDA

KAMRA Inlay - Overview

- Clinically meaningful improvement in uncorrected near vision with little or no compromise to distance vision
- Inlay provides an extended depth focus and although implanted monocularly, is fundamentally different than standard “monovision”
- Important new option for the surgical treatment of presbyopia, offering meaningful benefits

Presentation Agenda

Introduction	**Nick Tarantino, OD** *Chief Clinical & Regulatory Officer* *AcuFocus, Inc.*
Clinical Landscape	**Vance Thompson, MD** *Clinical Investigator*
Study Design	**Corina van de Pol, OD, PhD** *VP Clinical Research* *AcuFocus, Inc.*
Effectiveness	**John A Vukich, MD** *Clinical Investigator*
Safety	**Jay Pepose, MD, PhD** *Clinical Investigator*
Optimization of Surgical Procedure	**Dan Durrie, MD** *Clinical Investigator*
Benefit/Risk Conclusions	**John A Vukich, MD** *Clinical Investigator*

Experts

- David Evans, PhD – Visual Performance
- Chris Johnson, PhD – Visual Fields
- Lisa Keay, PhD – Patient Reported Outcomes
- Joel Verter, PhD – Statistics

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Clinical Landscape

Vance Thompson, MD

Clinical Investigator

Vance Thompson Vision

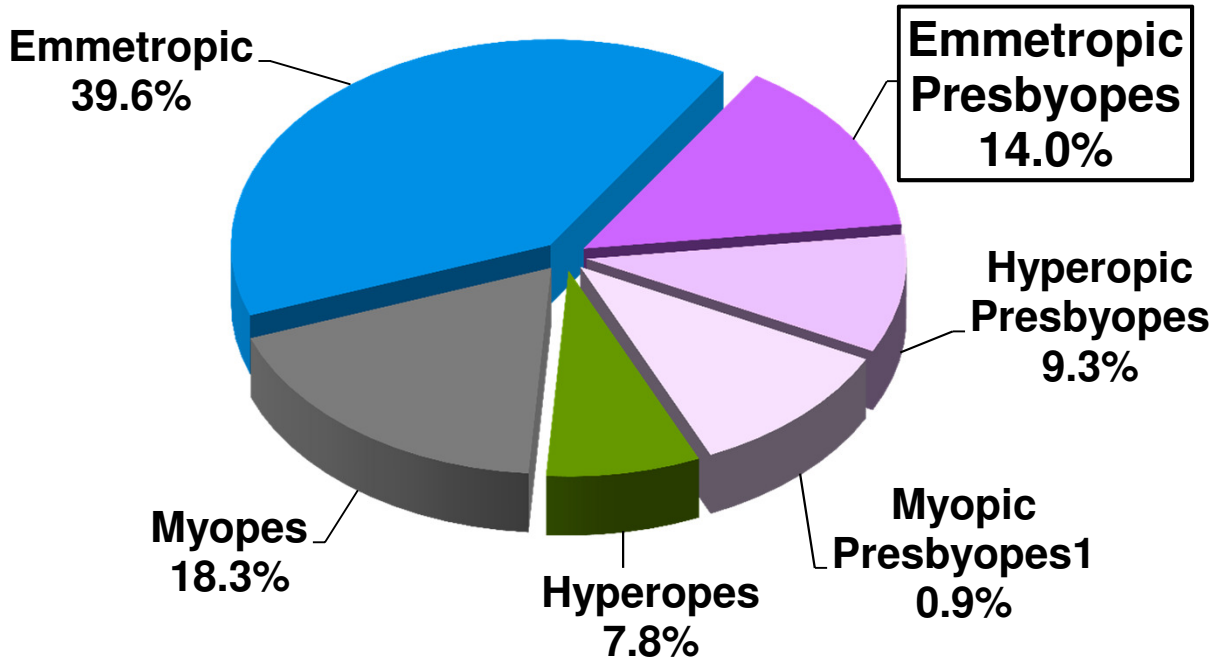
Sioux Falls, South Dakota

Overview of Clinical Landscape

- Presbyopia
- Current treatment options
- Rationale for KAMRA Inlay
- Surgical procedure

Presbyopia

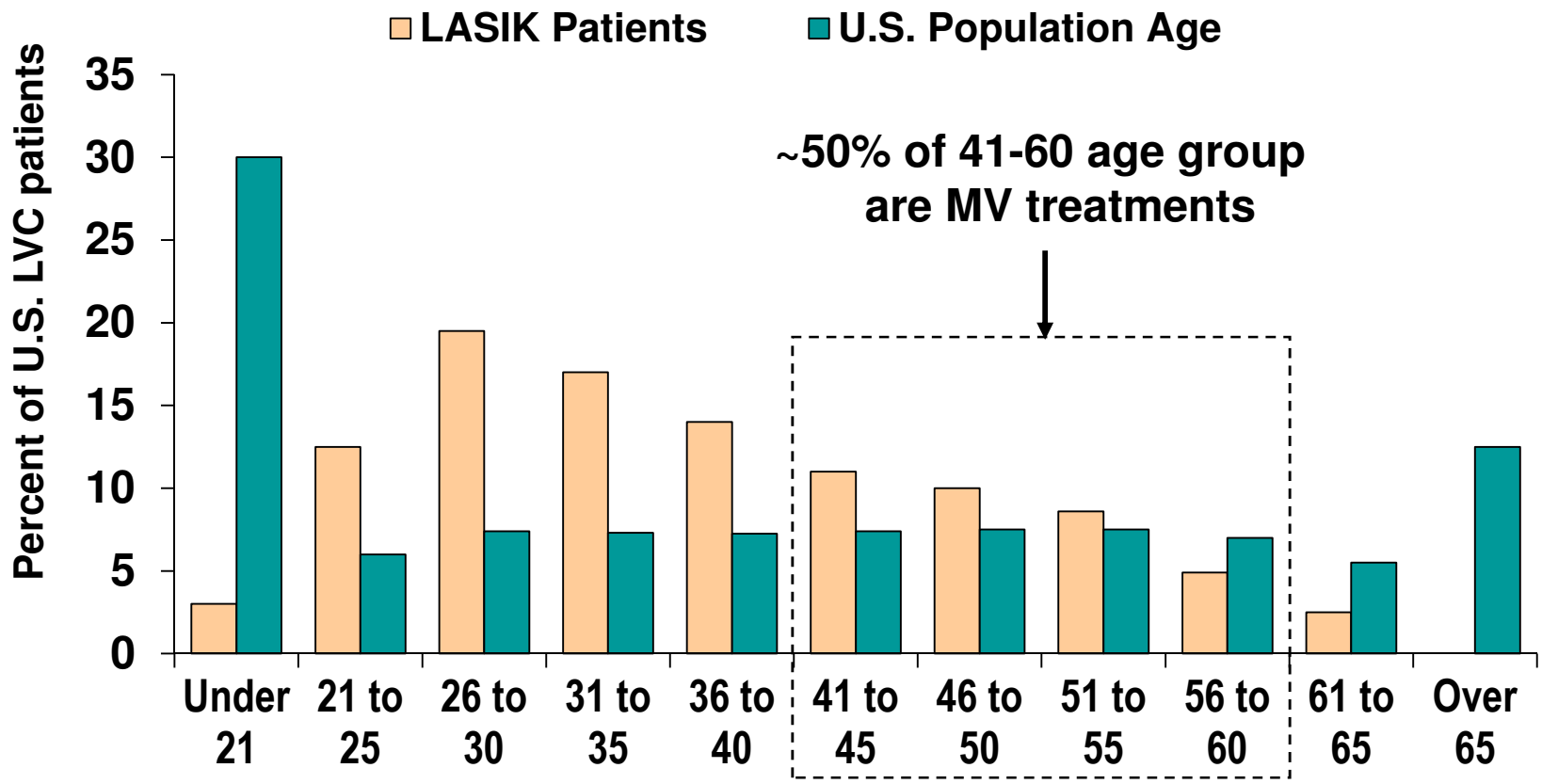
- Most common, universal ocular condition
- Over 80 million people age 45 to 64 in U.S.
  - 14% (~11 million) are emmetropic presbyopes



Data from 2012 update to 2010 census and 2014 Marketscope.

Age Profile of U.S. Laser Refractive Patients

- ~15% of all laser refractive ablations are monovision treatments



Data from 2014 Marketscope.

Presbyopes with Good Distance Vision

- Challenging population to satisfy
  - No history of spectacle use, so resistant to use of near correction with glasses or contact lenses
  - Reluctant to compromise distance vision for gain in near vision
  - No current treatment available to satisfy both

Surgical Correction of Presbyopia: Currently Limited to Monovision

- Conductive Keratoplasty (CK)
- Laser refractive surgery

A good surgical correction of presbyopia remains a significant unmet need

Presbyopia Corneal Surgery

- Growing interest in corneal inlays
- Removability

Corneal Correction of Presbyopia: Monovision

- An exercise in compromise
- What are you willing to give up at distance to help you at near?

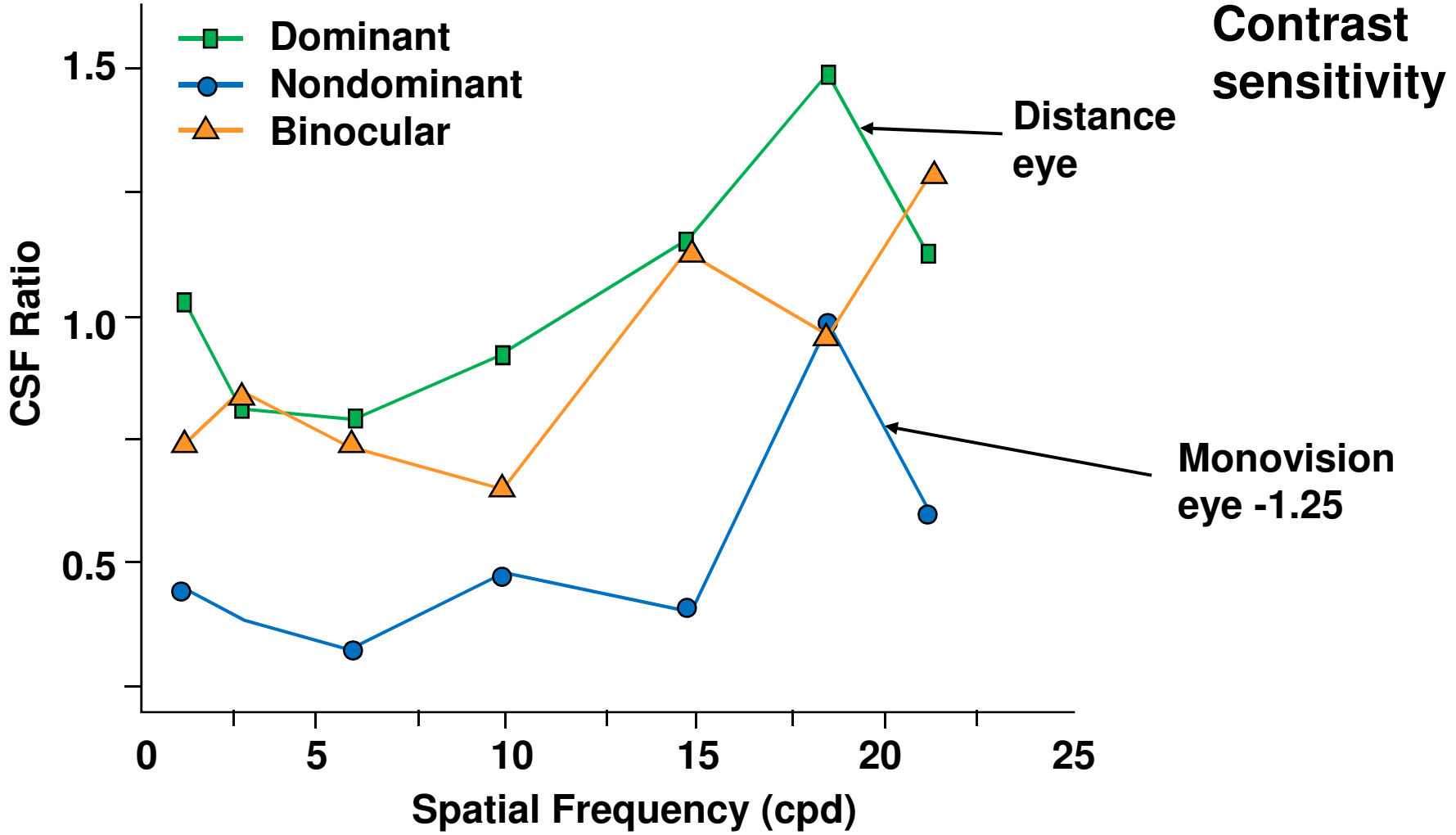
Visual Quality after Monovision LASIK
Aixa Alarcon, et al; JCRS Sept 2011

- **Lasik (25 patients):**
  - **Dominant:** plano
  - **Non-dominant:** -1.25
- **Analysis:** **Results**
  - **Visual acuity** improved near
  - **Contrast sensitivity** reduced
  - **Stereo acuity** reduced

significantly

Information not reviewed by FDA

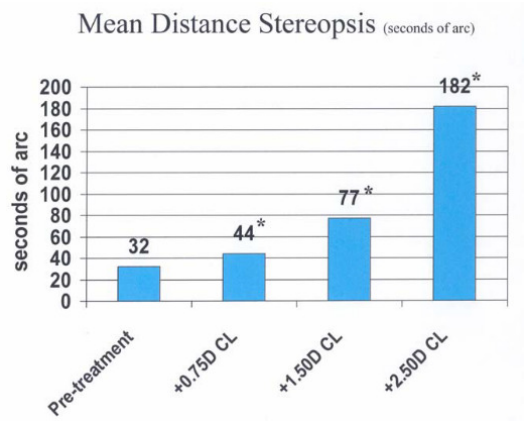
Visual Quality after Monovision LASIK
Aixa Alarcon, et al; JCRS Sept 2011



Information not reviewed by FDA

Contact Lens Monovision Reduction of Stereopsis

- **Prospective Study:**
  - **Durrie, Trans Am Ophthalmol Soc 2006:104:366-401**
- **Design:**
  - **Increasing levels of CL monovision**
  - **Distance stereo acuity test, Optec 3500**
- **Stereopsis (arc sec):**
  - **Baseline: 32 ± 23**
    - **+ 0.75 D: 44 ± 38, 1.38 fold increase**
    - **+ 1.5 D: 77 ± 76, 2.41 fold increase**
    - **+ 2.5 D: 182 ± 142, 5.7 fold increase**

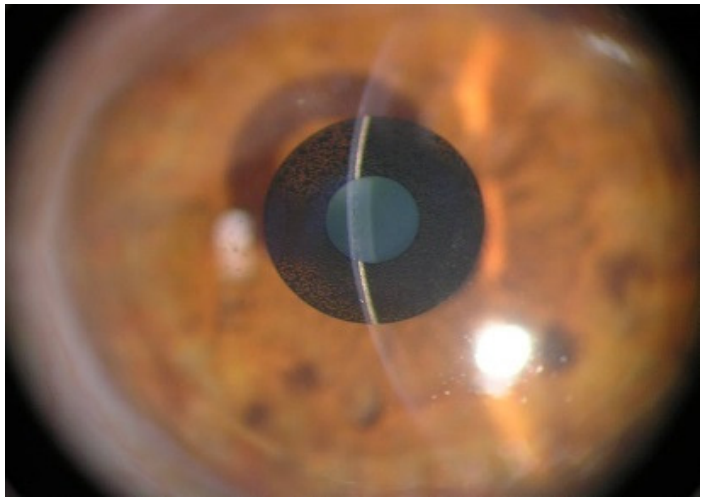


ALL changes are statistically significant: (p< 0.01)

Information not reviewed by FDA

KAMRA Inlay
Extended Depth of Focus

- Impressive near vision
- Depth of focus



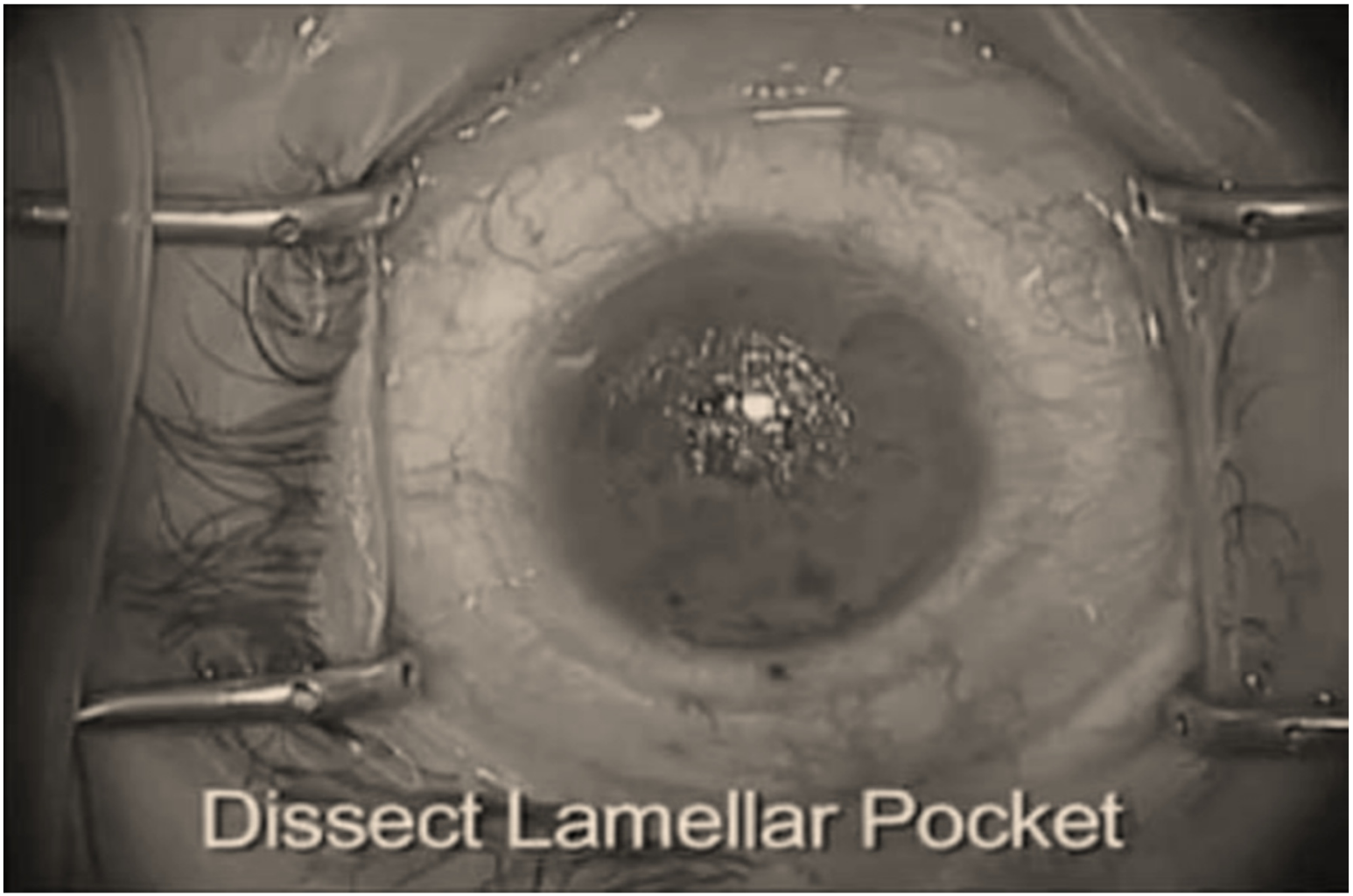
KAMRA Inlay Reading Vision

- Distance vision preserved
- Contrast sensitivity minimally reduced
- Removable
- Effect sustained with time
- Range of vision preserved

KAMRA Inlay Surgical Procedure

- Create a pocket in the cornea
  - Standard femtosecond laser setting used for LASIK procedures
  - Depth of ≥180 µm
- Inlay is easily positioned
- Procedure <10 min duration, minimal learning curve
- Postoperative topical antibiotics and corticosteroids

A Typical Pocket Procedure



Rationale for KAMRA Inlay

- Improve near vision, with little or no compromise to distance visual acuity, due to extended depth of focus
- Binocular vision maintained
- Reduce dependence on reading glasses
- Removable, in contrast to current surgical options
- Sustained effect over time

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Study Design

Corina van de Pol, OD, PhD

VP, Clinical Research
AcuFocus, Inc.

Pivotal Study Objective

- **Evaluate the safety and effectiveness of the KAMRA™ Inlay implanted intra-stromally in emmetropic presbyopes for improvement of near vision**

Pivotal Study Design

- Prospective, multi-center, open label, single-arm study
- Proposed sample size: 400 subjects
- Monocular implant
- Non-dominant eye
- 36 months with primary endpoints at 12 months

Confirmatory Study Design (020B)

- All lamellar resections in the confirmatory study were ≤6×6 spot/line separation
- 12 month study duration
- Proposed sample size 152 subjects
- Same effectiveness endpoints as pivotal study
- No intention to pool data with pivotal study

Key Inclusion Criteria

- Uncorrected near visual acuity (UCNVA) worse than 20/40 and better than 20/100
- Best corrected distance visual acuity better than or equal to 20/20 in both eyes
- Preoperative cycloplegic refractive spherical equivalent
  - +0.50 D to -0.75 D
  - ≤0.75 D of refractive cylinder
- Age: ≥45 and ≤60 yrs
- +1.00 D to +2.50 D of reading add
- Endothelial cell count ≥2000 cell/mm^2

Key Exclusion Criteria

- Anterior or posterior segment pathology
- Dry eye as determined by TBUT and Schirmer's Testing
- Taking chronic systemic medications known to exacerbate or induce moderate to severe dry eye
- Undergone previous intraocular or corneal surgery
- IOP >21 mmHg

Pivotal Study Investigators

24 sites: 15 US + 9 OUS sites

US Principal Investigators

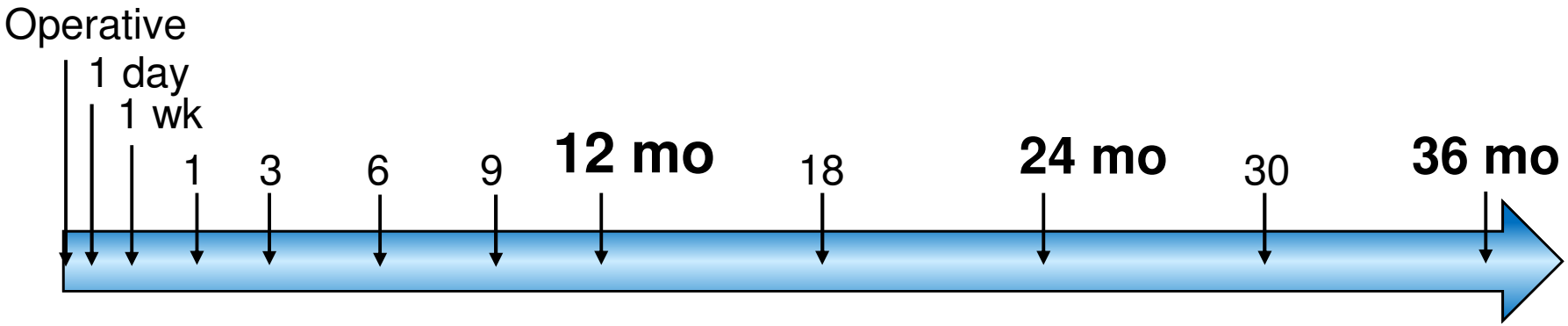
Stephen Coleman, MD
Daniel Durrie, MD
Gary Foster, MD
Peter Hersh, MD
Phillip Hoopes, Sr., MD
Colman Kraff, MD
Scott MacRae, MD, PhD
Robert Maloney, MD
Jay McDonald, MD
Jay Pepose, MD, PhD
Vance Thompson, MD
Thomas Tooma, MD
John Vukich, MD
Kevin Waltz, OD, MD
Jack Weiss, MD

OUS Principal Investigators

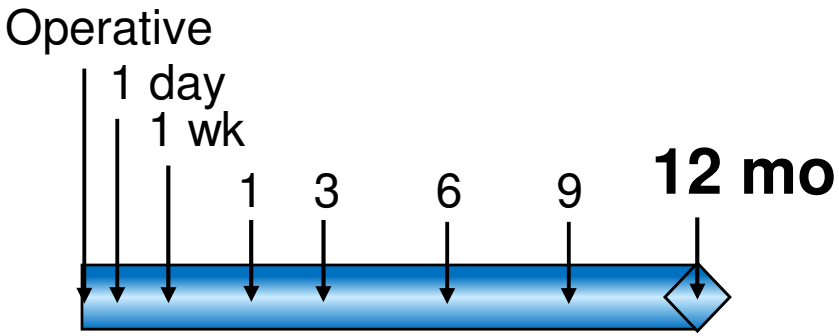
Robert Ang, MD - Philippines
Dean Corbett, MD - NZ
Burkhard Dick, MD - Germany
Günther Grabner, MD - Austria
David Kent, MD - NZ
Donald Tan, MD – Singapore
Jan Venter, MD - UK
Patrick Versace, MD - Australia
Rick Wolfe, MD – Australia

Study Examination Schedules

Pivotal Study:



Confirmatory Study:



Test Parameters

Vision Testing

- Manifest/Cycloplegic Refraction
- Uncorrected VAs:
  - Distance
  - Intermediate
  - Near
- Best-corrected VAs:
  - Distance
  - Intermediate
  - Near
- Contrast Sensitivity:
  - Photopic/Mesopic
  - With/Without Glare

Ocular Health

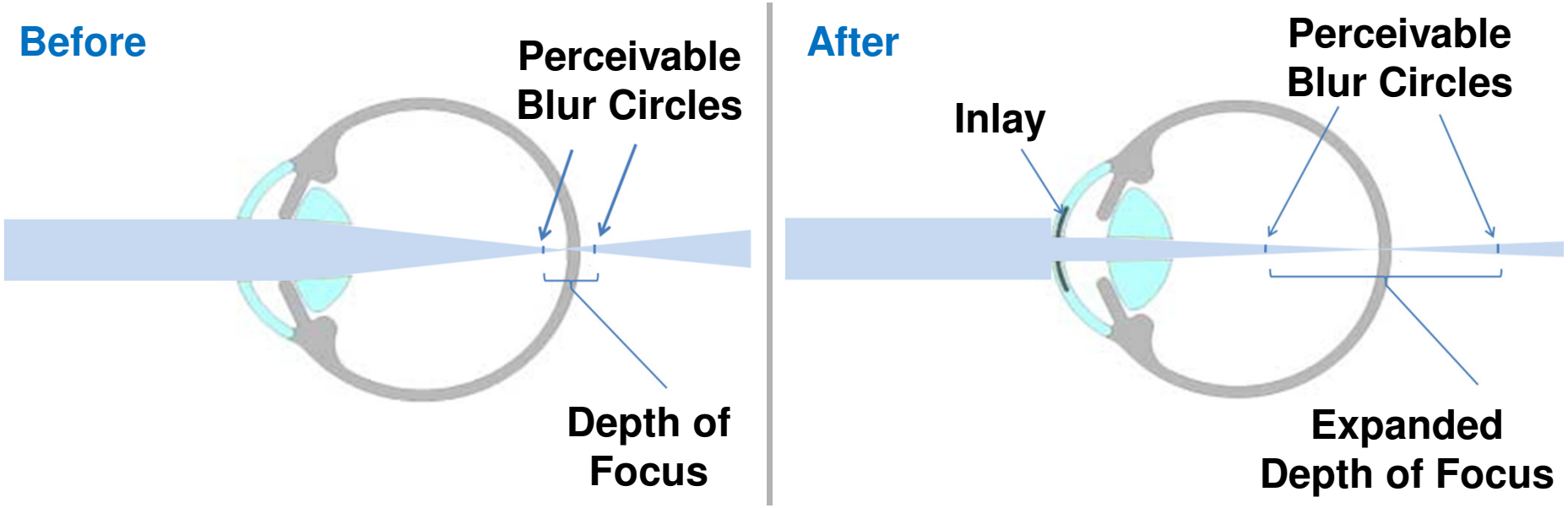
- Slit Lamp Biomicroscopy
- IOP Measurement
- Specular Microscopy
- Dilated Fundus Evaluation

Ancillary Testing

- Pachymetry
- Defocus Curves
- Visual Fields
- Corneal Topography
- Keratometry
- Patient-reported Outcomes

Postoperative Refractive Technique

- Mechanism of action of the inlay has an effect on the ability to determine a refractive endpoint
- Used “mid-point” refractions to establish arithmetic center of expanded depth of focus



Interobserver Repeatability of Refractions

- 3 different observers – repeated measures of refraction
- Proportion of agreement of MRSE*
  - Unimplanted eye
    - 86% ± 0.25 D
    - 98% ± 0.50 D
  - Implanted eye
    - 74% ± 0.25 D
    - 90% ± 0.50 D

* IDE G080184, Att 5.1.1.A

Effectiveness Endpoints

- **Primary effectiveness**
  - **75%* of implanted eyes should achieve uncorrected near visual acuity of 20/40 or better at 12 months**
- **Secondary effectiveness**
  - **Subjective improvement in near vision as measured by subject satisfaction questionnaire**
    - **Self-administered**
    - **Descriptive endpoint**
    - **Not intended to support labeling claims**

* Lower bound of 2-sided 95% CI.

Refractive Stability Endpoint

- ≥95% of eyes have a change of ≤1.00 D of MRSE between two refractions performed at least 3 months apart
- Mean rate of change in MRSE, as determined by paired analysis, ≤0.5 D per year (0.04 D/month) over the same time period
- Mean rate of change of MRSE decreases monotonically over time, with a projected asymptote of zero or a rate of change attributable to normal aging
- 95% CI for the mean rate of change includes zero or a rate of change attributable to normal aging

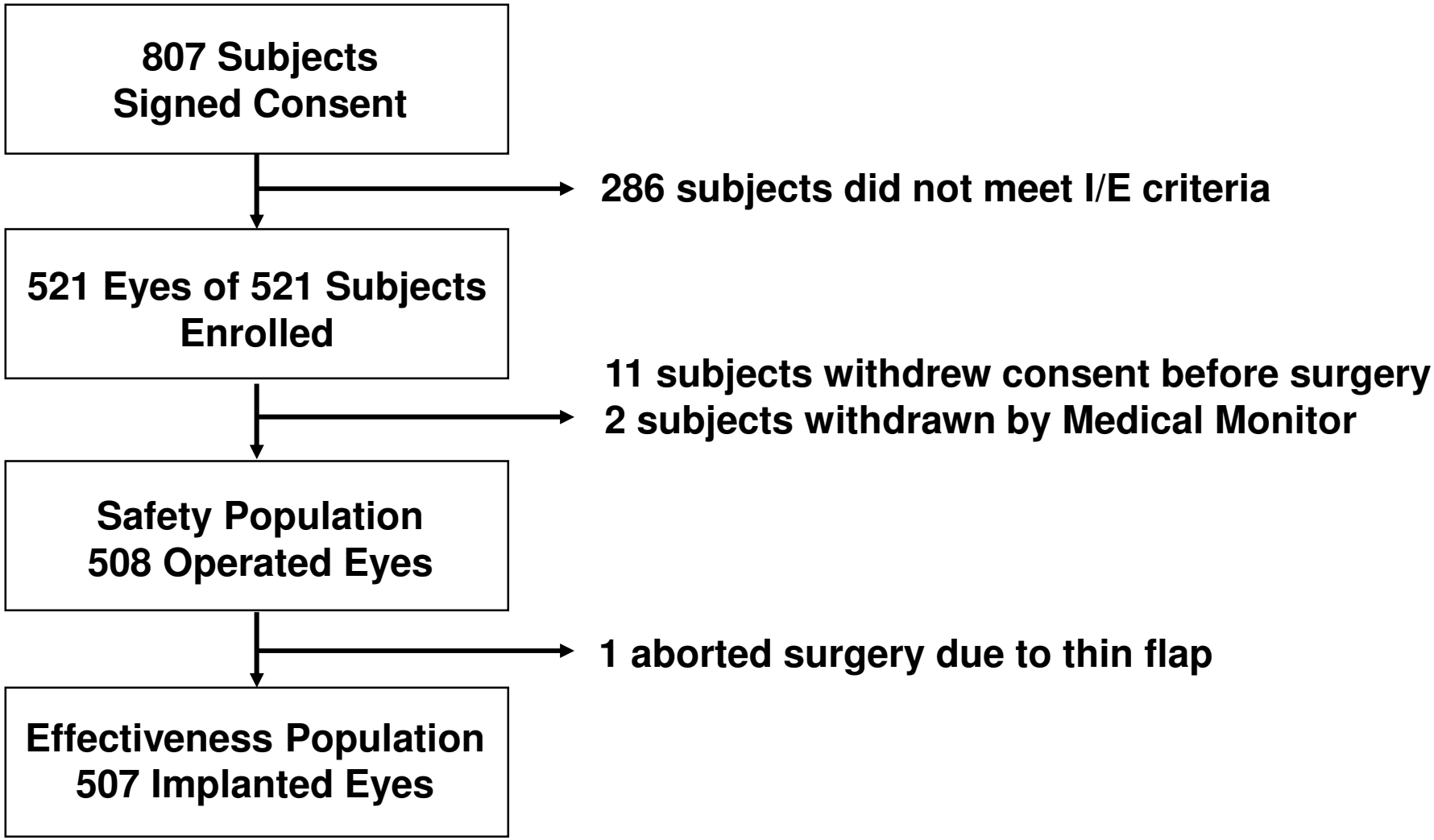
Safety Endpoints

- **Preservation of BCDVA**
  - **<5% of eyes with persistent loss of 2 lines or more of BCDVA at 12 months**
  - **<1% of eyes with preoperative BCDVA of 20/20 with BCDVA worse than 20/40 at 12 months**
  - **<1% of eyes with clinically significant corneal haze on slit lamp examination, as associated with decrease in BCDVA of >2 lines not due to irregular astigmatism, at 12 months**

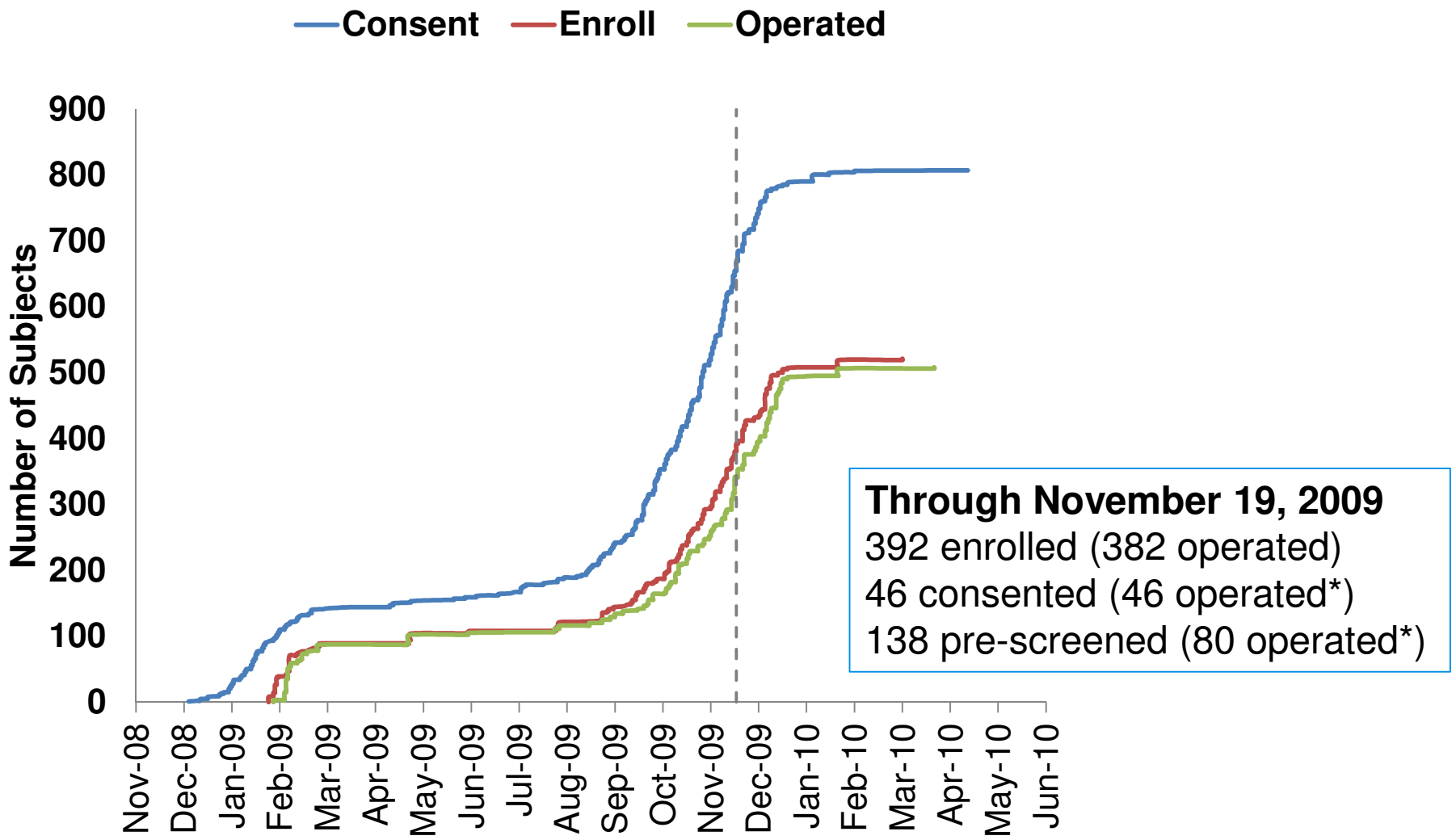
Safety Endpoints (cont.)

- **Induced manifest refractive astigmatism**
  - **<5% of eyes with induced manifest refractive astigmatism >2.00 D at 12 months**
- **Cumulative incidence of AEs**
  - **Device-related AEs in ≤5% of eyes**
  - **Any single device-related AE in ≤1% of eyes**

Study Enrollment



Study Enrollment



*After November 19, 2009

Poolability

- First 400 and next 121 subjects are poolable from outcomes point of view but not baseline characteristics
- Justified by consistent study conduct
- Same:
  - Study design
  - Study conduct
  - Training
  - Procedure
  - Inclusion/exclusion criteria
  - Sites
  - Data collection
  - Data monitoring/audits

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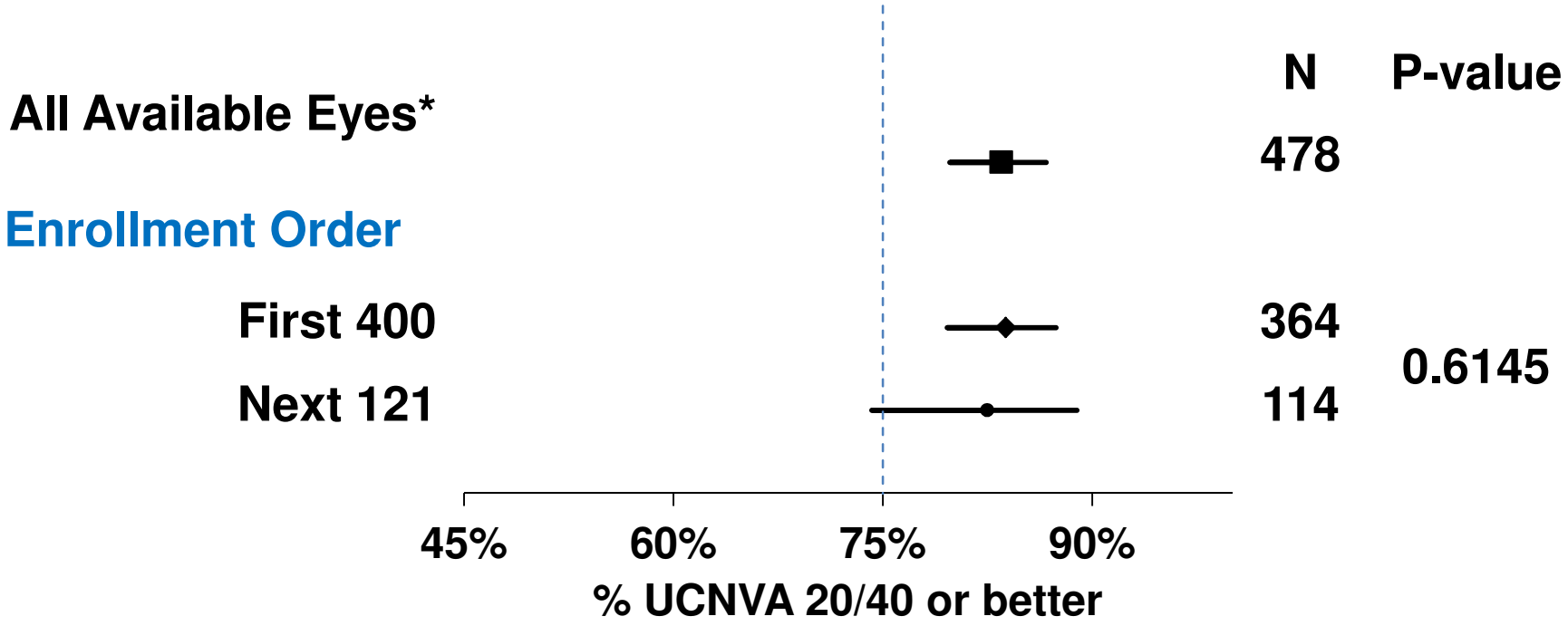
Enrollment Order

- Effectiveness criteria met for first 400 eyes
- Effectiveness of eyes enrolled after 400, not different
- No interim analysis to drive additional 121 eyes



*All available eyes for effectiveness at 12 months.

Demographics

	Subjects n (%)
Age (yrs)	**N = 508**
Mean (SD)	52 (4)
min, max	45, 60
Gender	
Male	240 (47.2)
Female	268 (52.8)
Surgical Eye	
Right	176 (34.6)
Left	332 (65.4)
Race	
White	449 (88.4)
Asian	26 (5.1)
Hispanic	25 (4.9)
Black	4 (0.8)
Other	4 (0.8)

Study Compliance

- Available for analysis
  - 94.3% (479/508) at Month 12
  - 87.0% (442/508) at Month 24
  - 83.5% (424/508) at Month 36
- Discontinuations, n = 49 (9.6%) through Month 36
  - 44 removals
  - 4 exited due to lenticular changes (cataracts)
  - 1 not implanted
- Lost to follow-up: n = 35 (6.9%) through Month 36
- Protocol deviations: 0.71% (777/109,274*)

* Total cumulative test or visits over course of study.

Protocol Deviations - Definitions

- FDA guidance on International Conference on Harmonization – (ICH E3)
- Major protocol deviation
  - Might significantly affect the completeness, accuracy and/or reliability of the study data
  - Might significantly affect a subject's rights, safety or well-being
- Minor protocol deviation
  - All other deviations

Protocol Deviations – Major Deviations

Deviation	Number of Deviations	% of Total Possible
Inclusion / Exclusion	32	6.1
Missed / Incorrect Assessment Related to Key Safety or Effectiveness	13	0.04 - 0.17
Other	9	0.20 - 1.15
Total	54	0.24

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Protocol Deviations – Minor Deviations

Deviation	Number of Deviations	% of Total Possible
Missed Visit	170	2.9
Out-of-Window Visit	158*	2.8
Missed / Incorrect Assessment Not Related to Key Safety or Effectiveness	393	0.06 - 4.34
Other	2	0.20
Total	723	0.84

*19 PDs related to out of window visits at Month 12

Summary

- Subject accountability was good
- Enrollment beyond 400 did not positively bias the study outcomes
- Determination of refractive stability is affected the decreased repeatability of refractions with an increased depth of focus
- Overall rate of protocol deviations – 0.71% of total possible study data points

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Effectiveness Results

John A Vukich, MD

Clinical Investigator

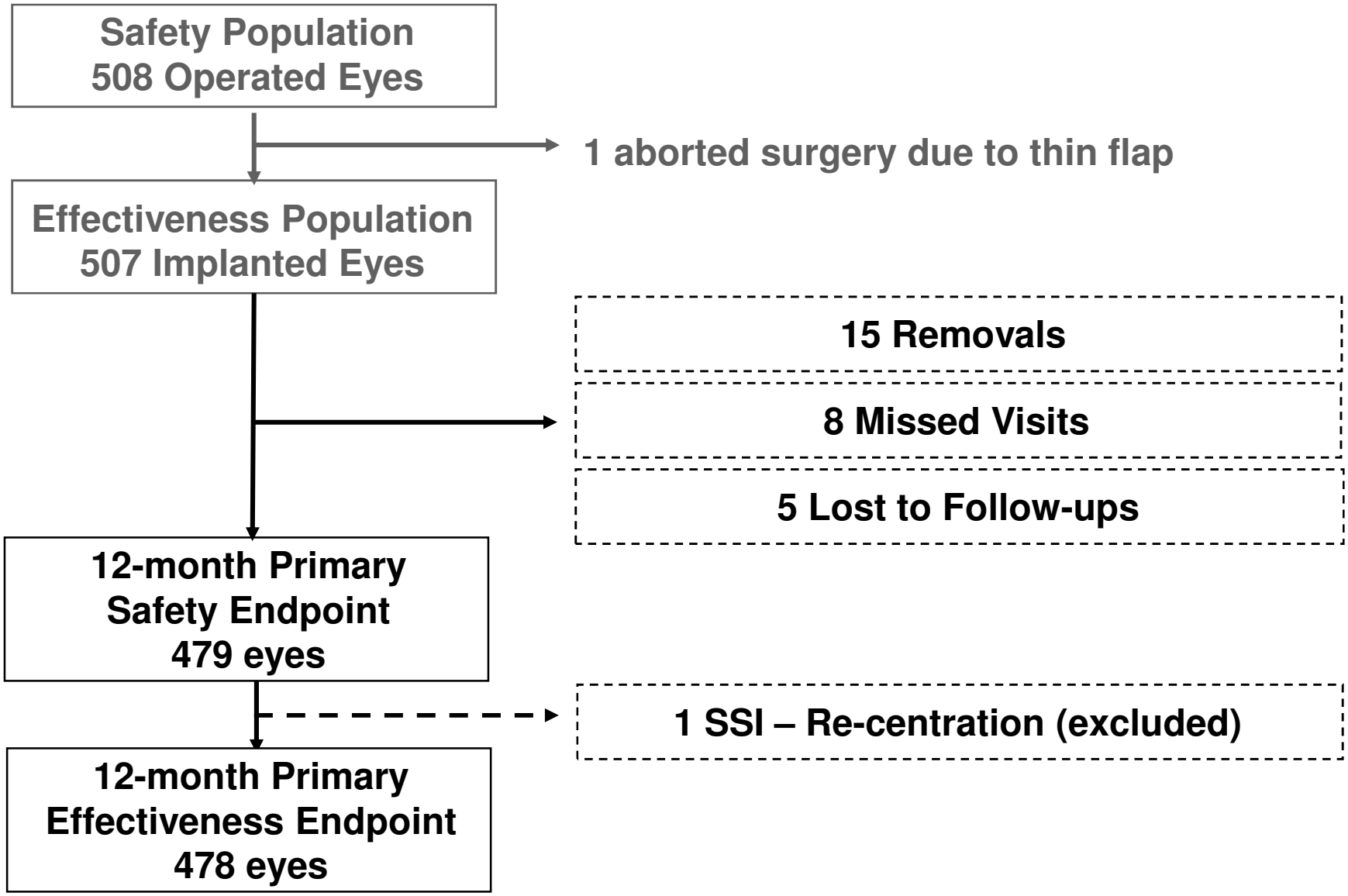
Davis Duehr Dean

Madison, Wisconsin

Effectiveness Outcomes

- Primary effectiveness endpoint
- Secondary effectiveness endpoint
- Refractive stability

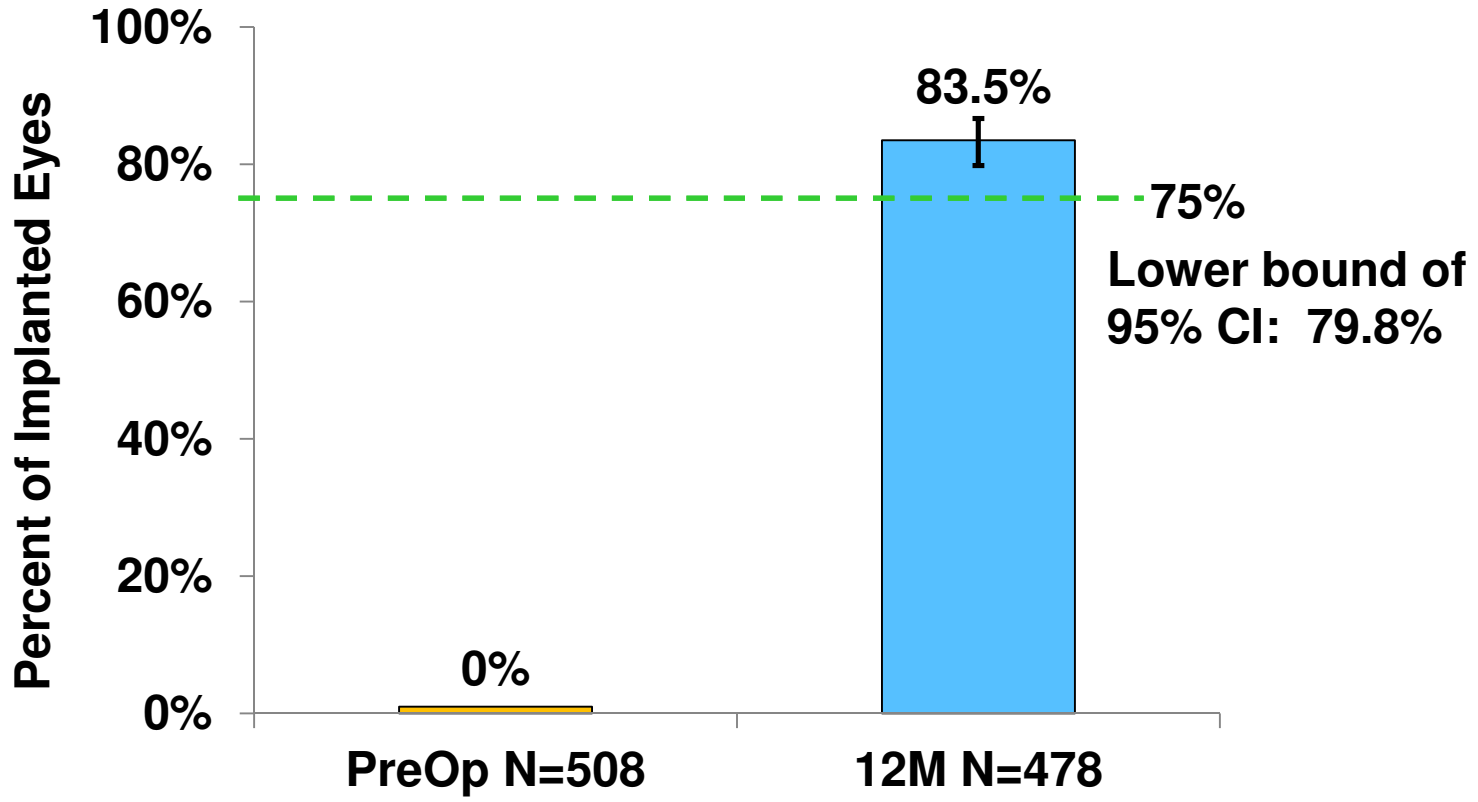
Effectiveness Population at 12 Months



Primary Effectiveness

Primary Effectiveness Endpoint

- 75% of eyes should achieve UCNVA of 20/40 or better at 12 months



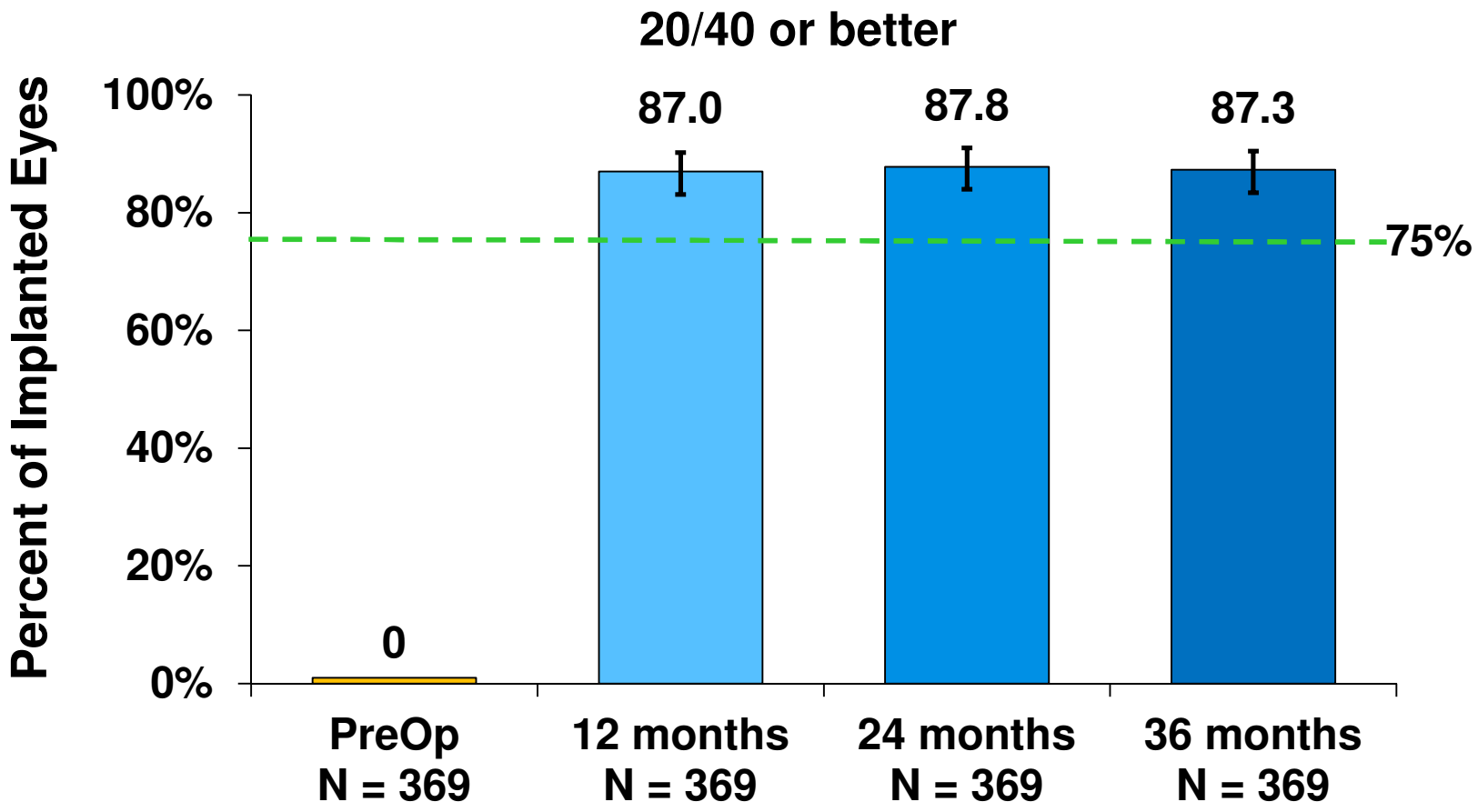
Imputation Results at 12 Months

Percent estimate and CI of Primary Effectiveness endpoint

	Primary Endpoint Analysis	Imputation Analysis			
	Available Data	Tipping Point	Best Case	Worst Case	Last Observed
N	478	507	507	507	507
n (20/40 or better)	399	400	411	403	409
% (20/40 or better)	83.5%	78.9%	81.1%	79.5%	80.7%
Lower bound of 95%CI*	79.8%	75.1%	77.4%	75.7%	77.0%

*Exact Binomial method used to calculate the CI for the percent estimate.

Primary Effectiveness Endpoint: 36 Months Consistent Cohort



Analysis not previously submitted to FDA

Small-gauge, sutureless pars plana vitrectomy to manage vitreous loss during phacoemulsification

K.V. Chalam, MD, Shailesh K. Gupta, MD, Sanjay Vinjamaram, MD, Vinay A. Shah, MD

This technique is useful during phacoemulsification with posterior capsule rupture during phacoemulsification. A self-sealing limbal incision is made with a sutureless, self-sealing incision performed in a closed chamber, maintaining normal intraocular pressure. A high-speed cutter exerts minimal traction on the vitreous. Accessibility to the vitreous through the pars plana is better, ensuring more complete removal of the vitreous and restoration of normal anatomy.

J Cataract Refract Surg 2003; 29:1482–1486 © 2003 ASCRS and ESCRS

Vitreous loss during cataract surgery leads to immediate and long-term complications with potentially severe consequences. Despite surgical advances, the best corrected visual acuity after vitreous loss is worse than after uneventful cataract surgery.[1]

Phacoemulsification has become the predominant method of cataract extraction in the United States, used in 91% of cases.[2] With advances in phacoemulsification techniques, instrumentation, and intraocular lenses (IOLs), complications of cataract surgery with IOL implantation have continued to decline. The reported incidence of vitreous loss varies from 1.8% to 10% depending on the level of surgical training.[3]

Several strategies have been described for the management of vitreous loss.[4–8] We report a technique to manage vitreous loss during phacoemulsification using a sutureless, 25-gauge, high-speed vitrectomy system (1500 cuts/minute). The technique preserves the benefits of closed intraocular microsurgery[9] (Figures 1 and 2).

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None of the authors has a financial or proprietary interest in any material or method mentioned.

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0886-3350/03/$–see front matter
doi:10.1016/S0886-3350(03)00577-4

Surgical Technique

This technique is useful during phacoemulsification if the posterior capsule ruptures and the vitreous prolapses after nucleus removal.

Step 1: Creation of Corneal Wound

Upon recognition of vitreous prolapse, further phacoemulsification is immediately stopped. The corneal wound is secured with a single 10-0 polyglactin 910 suture (Vicryl®) to create a watertight anterior chamber (Figure 3). The corneal suture placement is left to the surgeon's discretion.

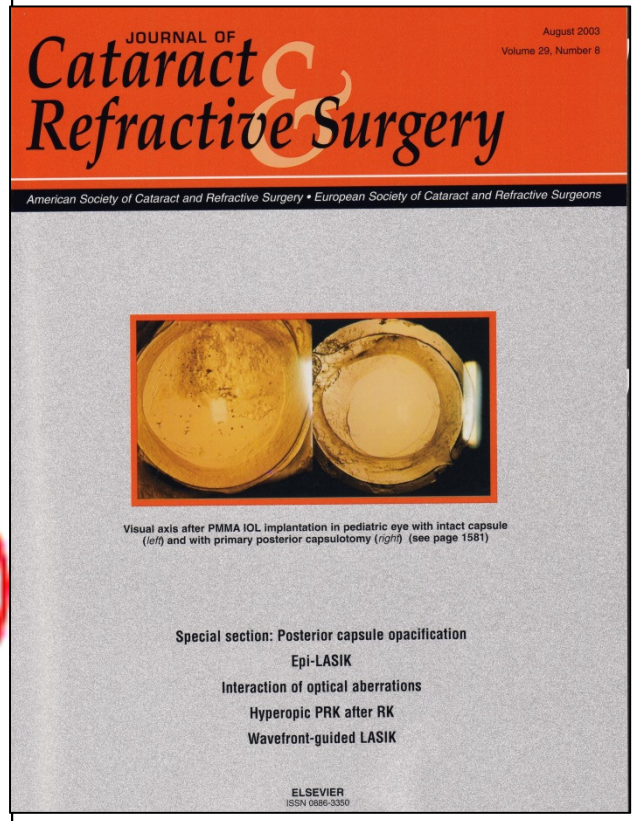
Step 2: Clearing the Corneal Wound of Vitreous

An additional self-sealing limbal incision is made with a diamond knife (1.0 mm) opposite the side of the previous port of entry. Through a side port, a 25-gauge infusion cannula is introduced, but the infusion is not opened. A second port is used to introduce an iris spatula. The corneal wound (tunnel) is cleared of vitreous strands by several sweeping movements with the spatula away from the wound toward the pupil (Figure 4). Complete removal of vitreous from the wound is confirmed with scleral illumination by a 25-gauge light pipe.

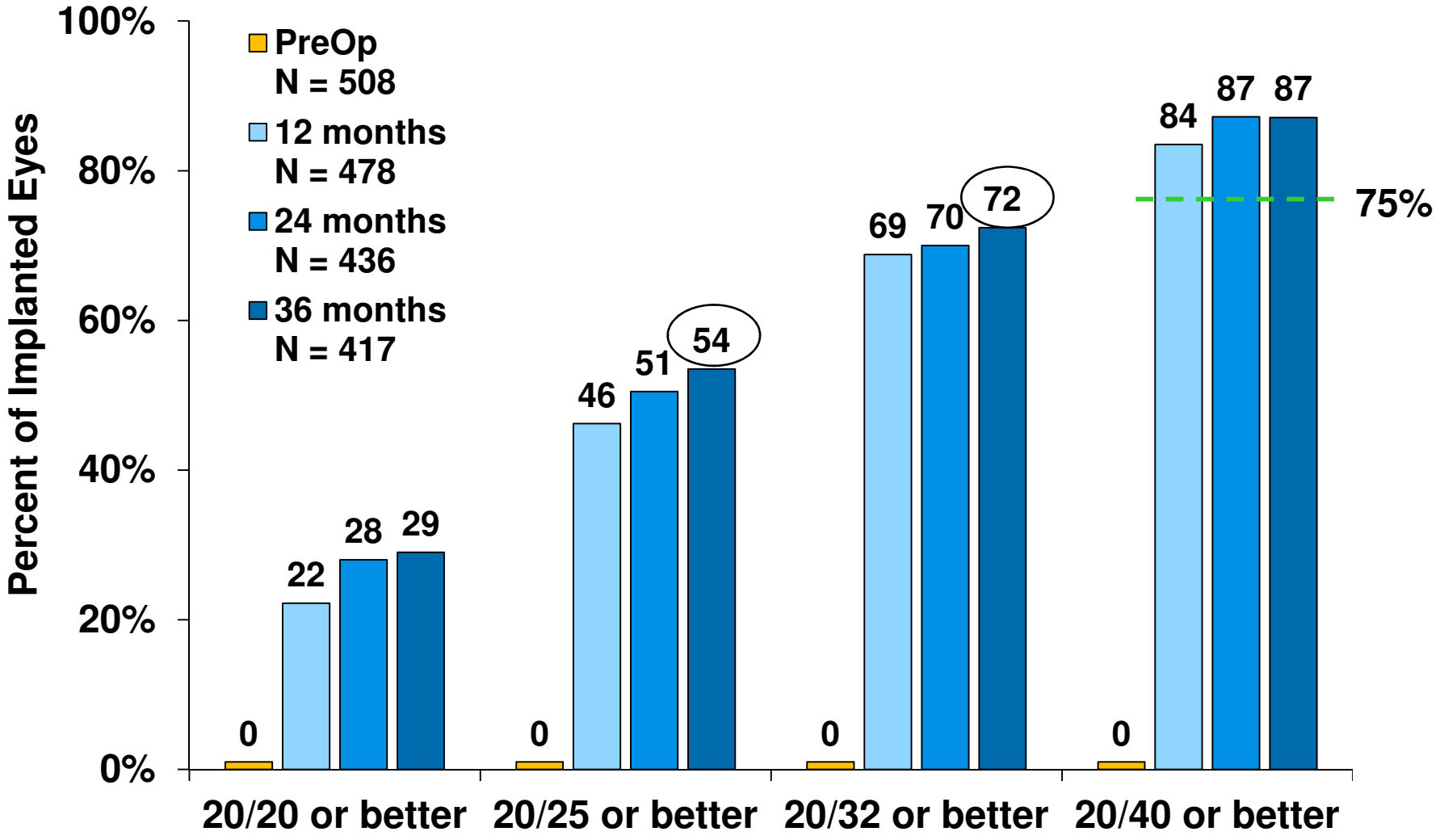
Step 3: Infusion Through a 25-Gauge Cannula

Once the wound is cleared of vitreous and the eye is a closed chamber, the 25-gauge infusion cannula is

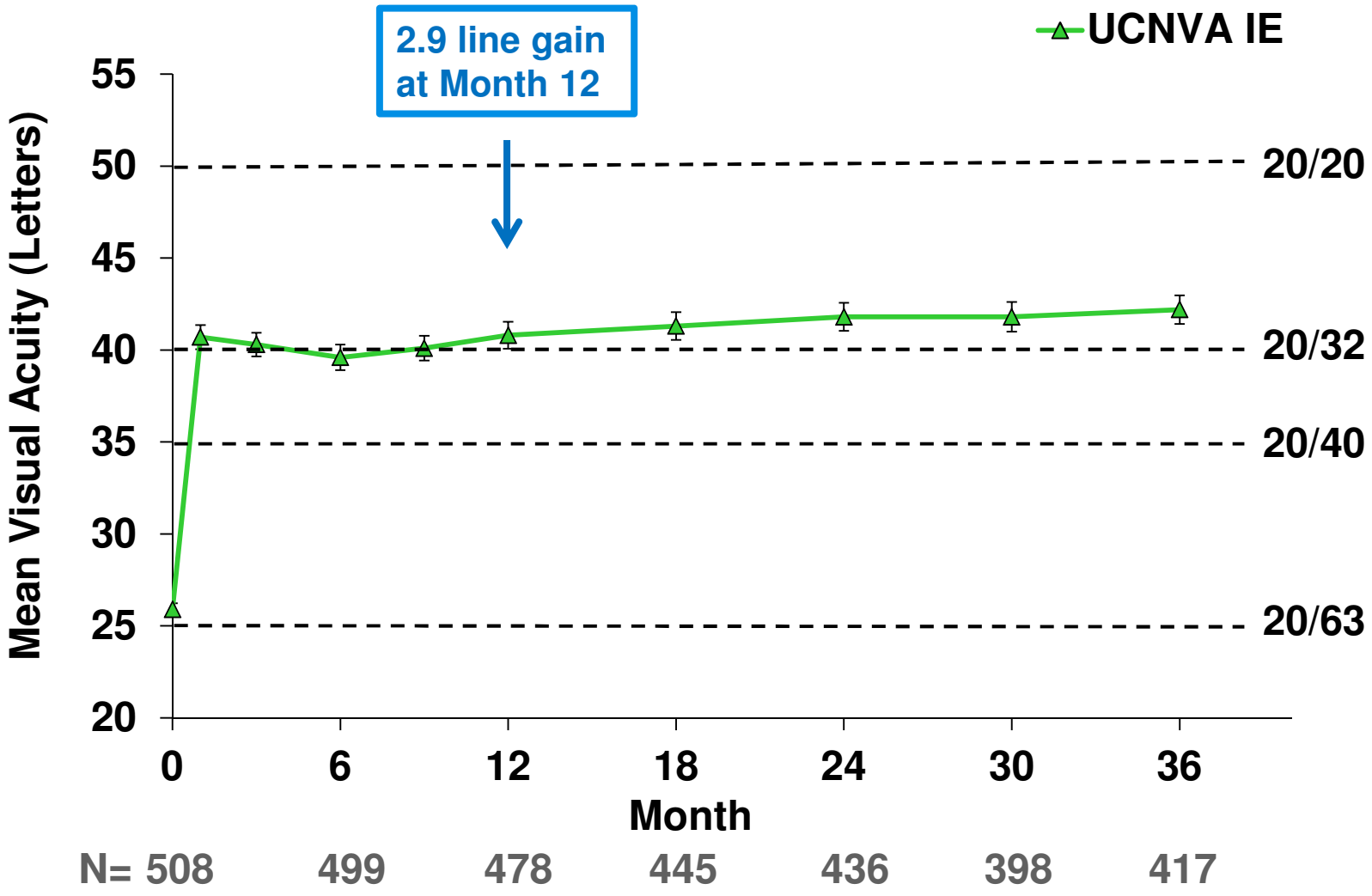
20/40
(8 point font)



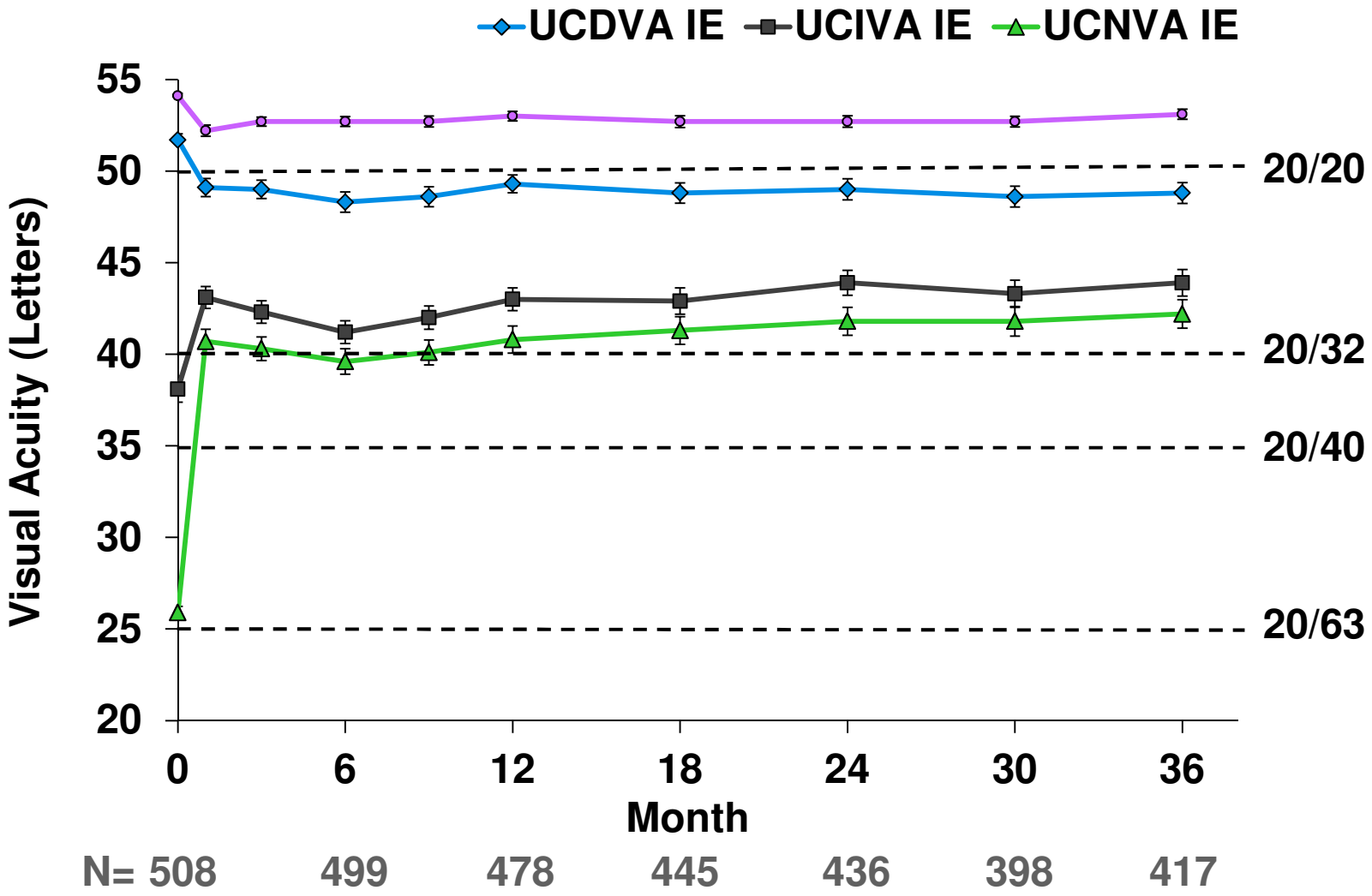
Monocular UCNVA at 12, 24, and 36 Months



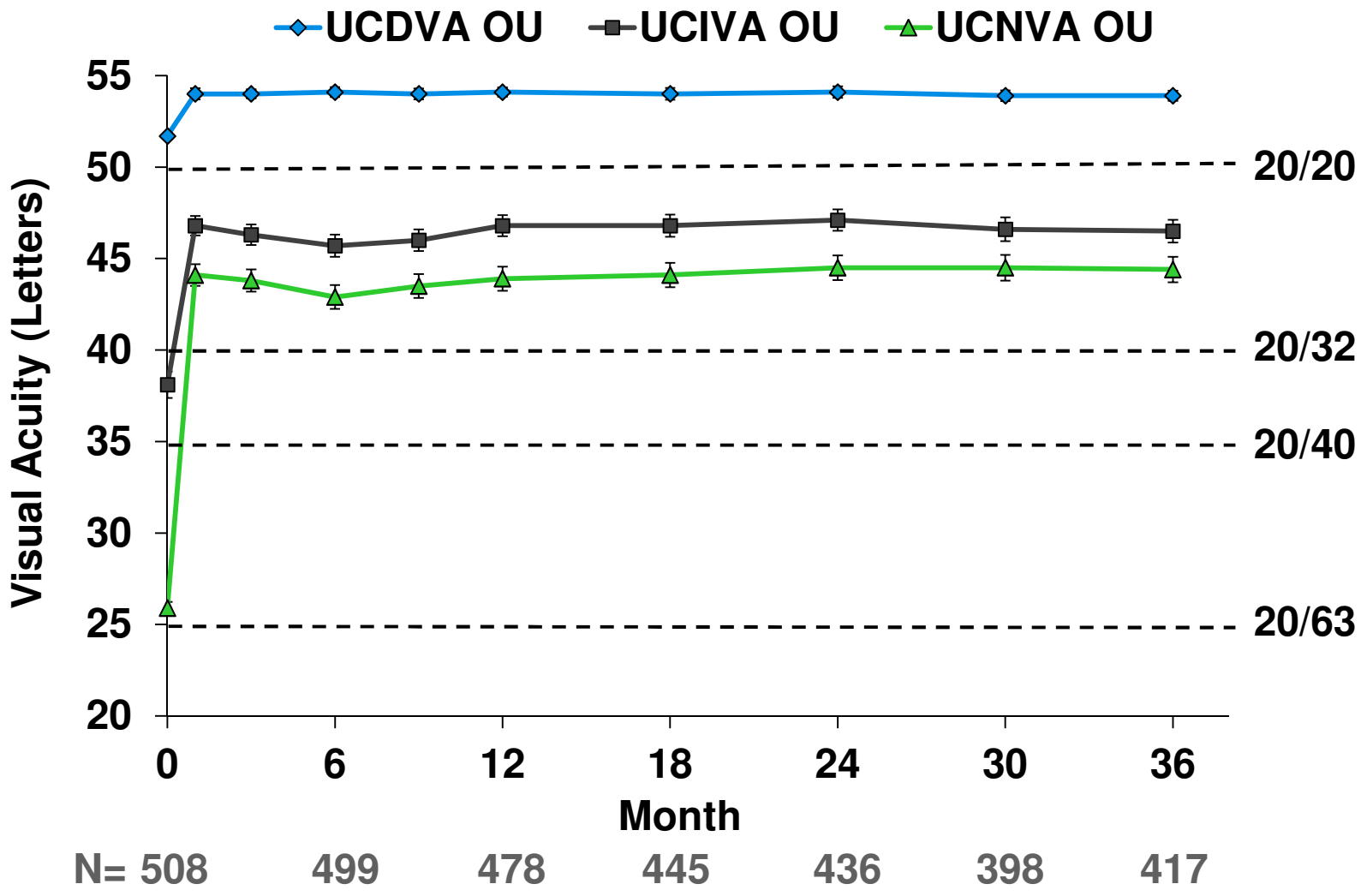
Monocular UCNVA: Implanted Eyes



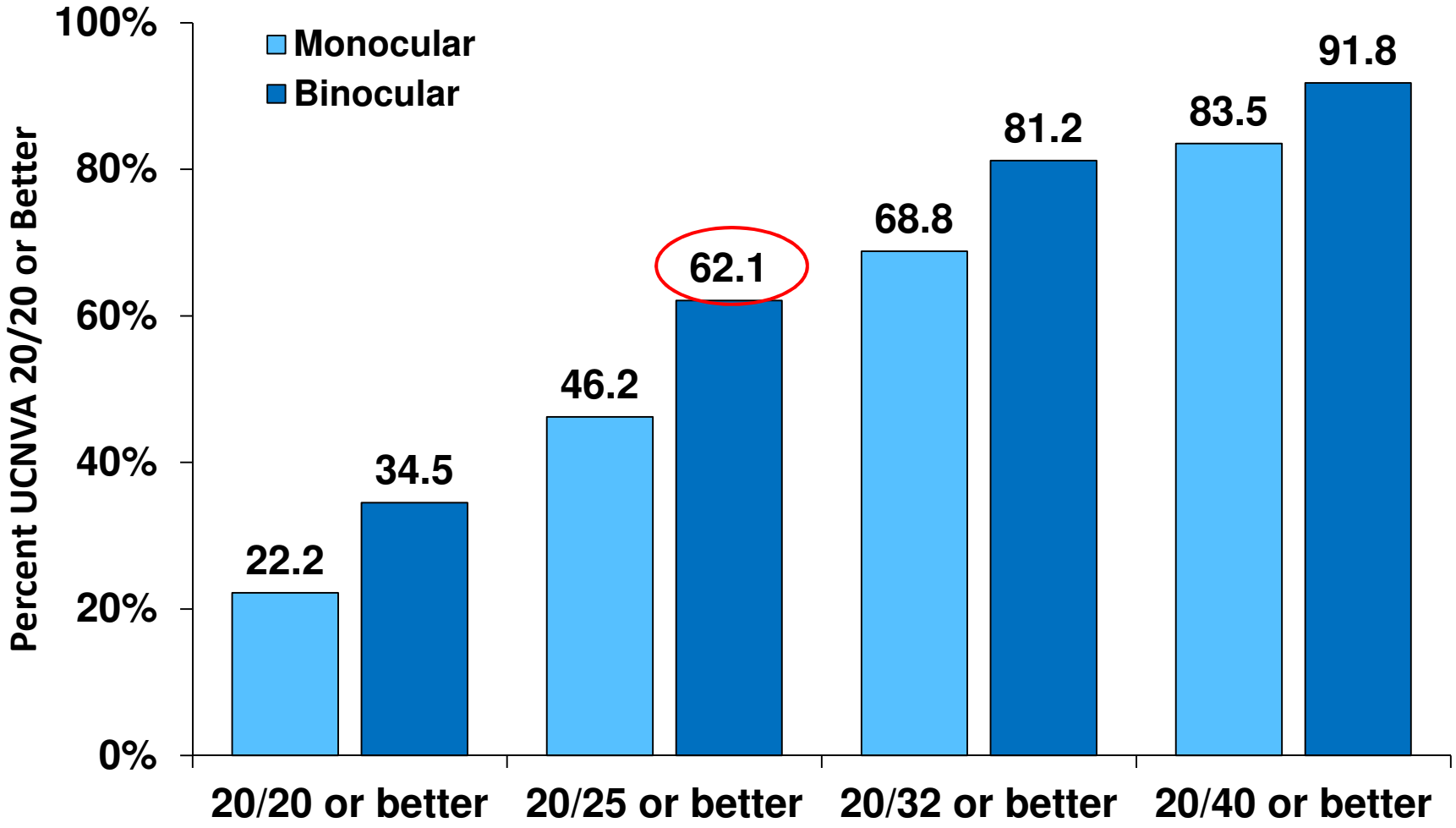
Monocular Distance, Intermediate, and Near Visual Acuities: Implanted Eyes



Binocular Distance, Intermediate, and Near Visual Acuities



Monocular and Binocular UCNVA: 12 Months



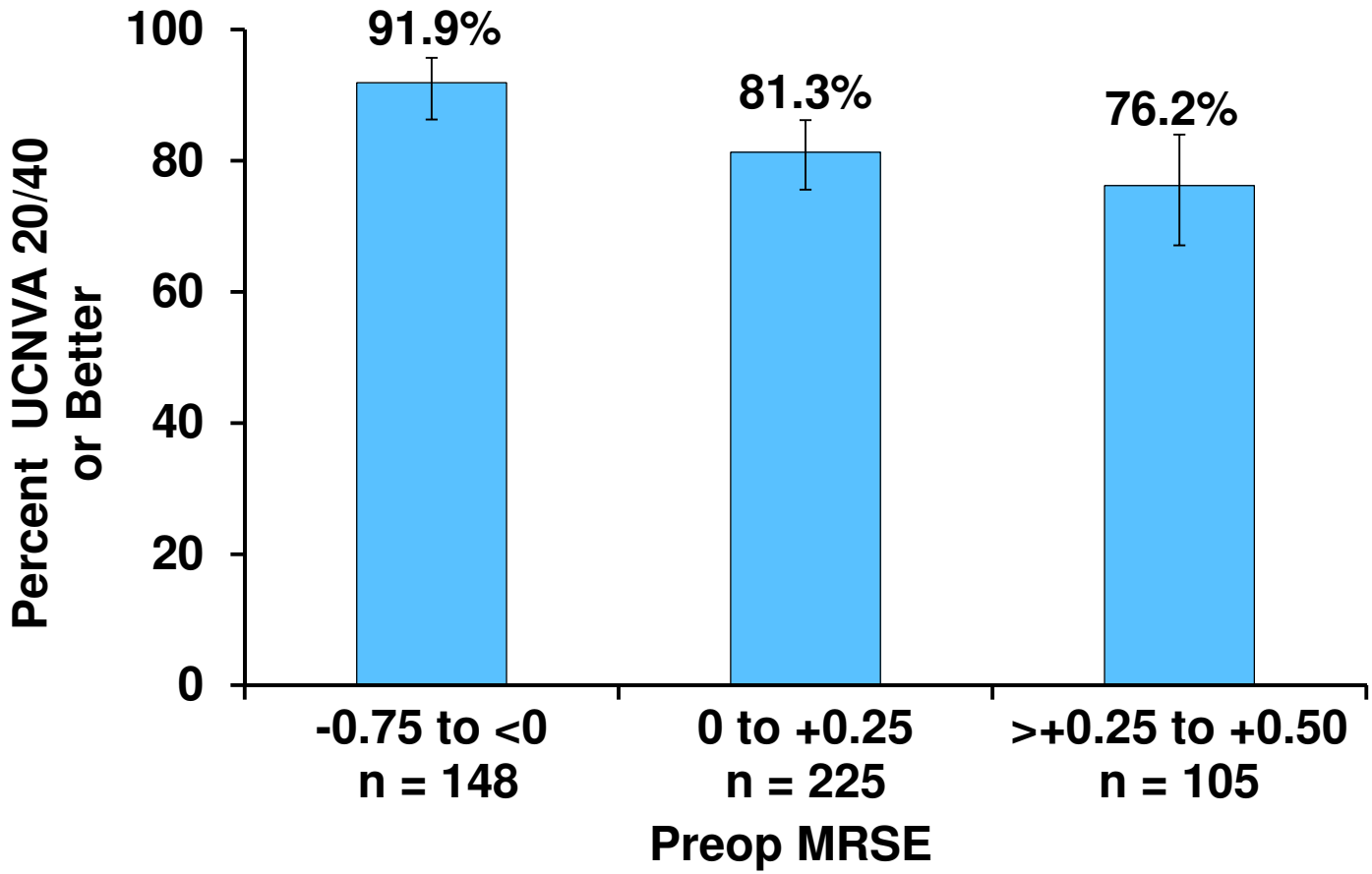
Exploratory Analysis to Identify Factors Related to Primary Effectiveness Outcome

- Site
- Demographic parameters:
  - Age, Gender, Race, US vs. OUS
- Baseline parameters:
  - UCNVA, MRSE, Near Add, Photopic and Mesopic Pupil Size, Keratometry, Central Corneal Thickness, ECD
- Surgical parameters:
  - Keratome type, pocket vs flap, depth of placement, implanted eye, surgical order, femtosecond laser settings (including ≤6×6 vs. non-6×6)

Primary Effectiveness Outcome by Baseline and Surgical Parameters

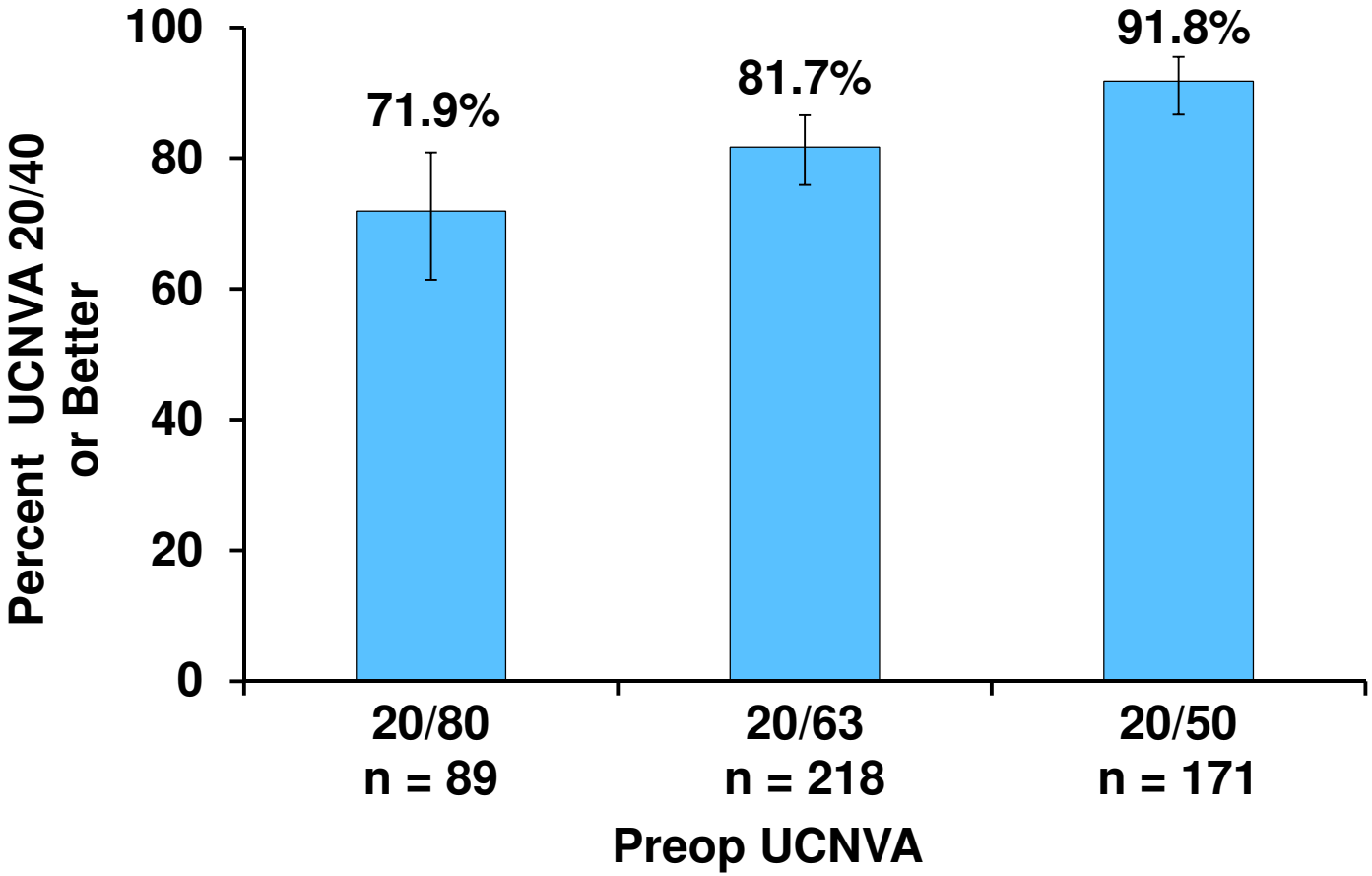
- 4 of 23 baseline and surgical parameters demonstrated significance by logistic regression analysis
  - Patient selection:
    - Preoperative MRSE
    - Preoperative UCNVA
    - Preoperative Photopic Pupil Size
  - Surgical technique:
    - ≤6×6 vs. non-6×6 femtosecond laser settings

Primary Effectiveness Endpoint at 12 Months Stratified by Preop MRSE



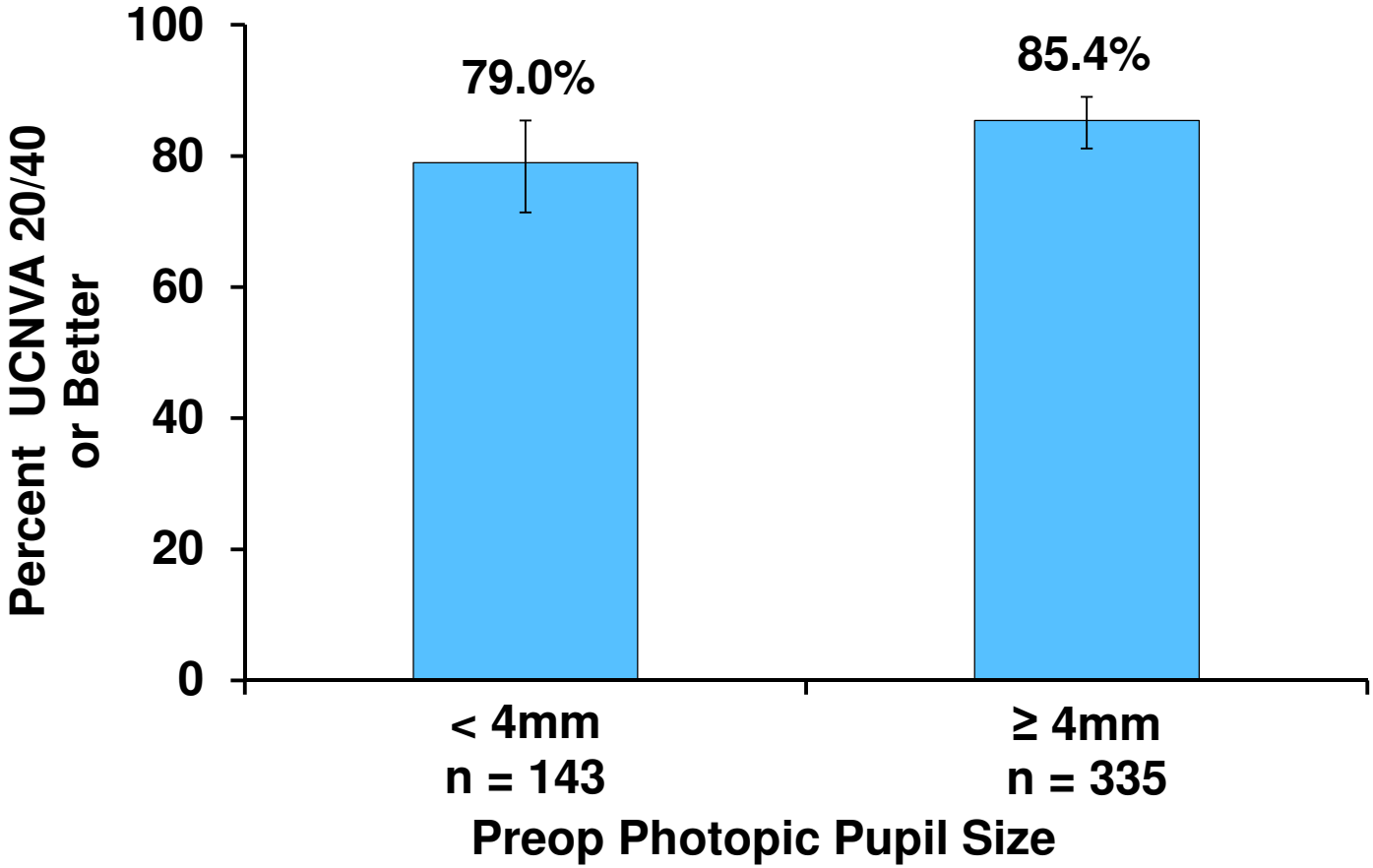
Mean UCNVA (SD):	44.0 (7.5)	40.2 (8.1)	37.3 (7.9)
Lines Improved (SD):	+3.3 (1.5)	+2.9 (1.6)	+2.6 (1.6)

Primary Effectiveness Endpoint at 12 Months Stratified by Preop UCNVA



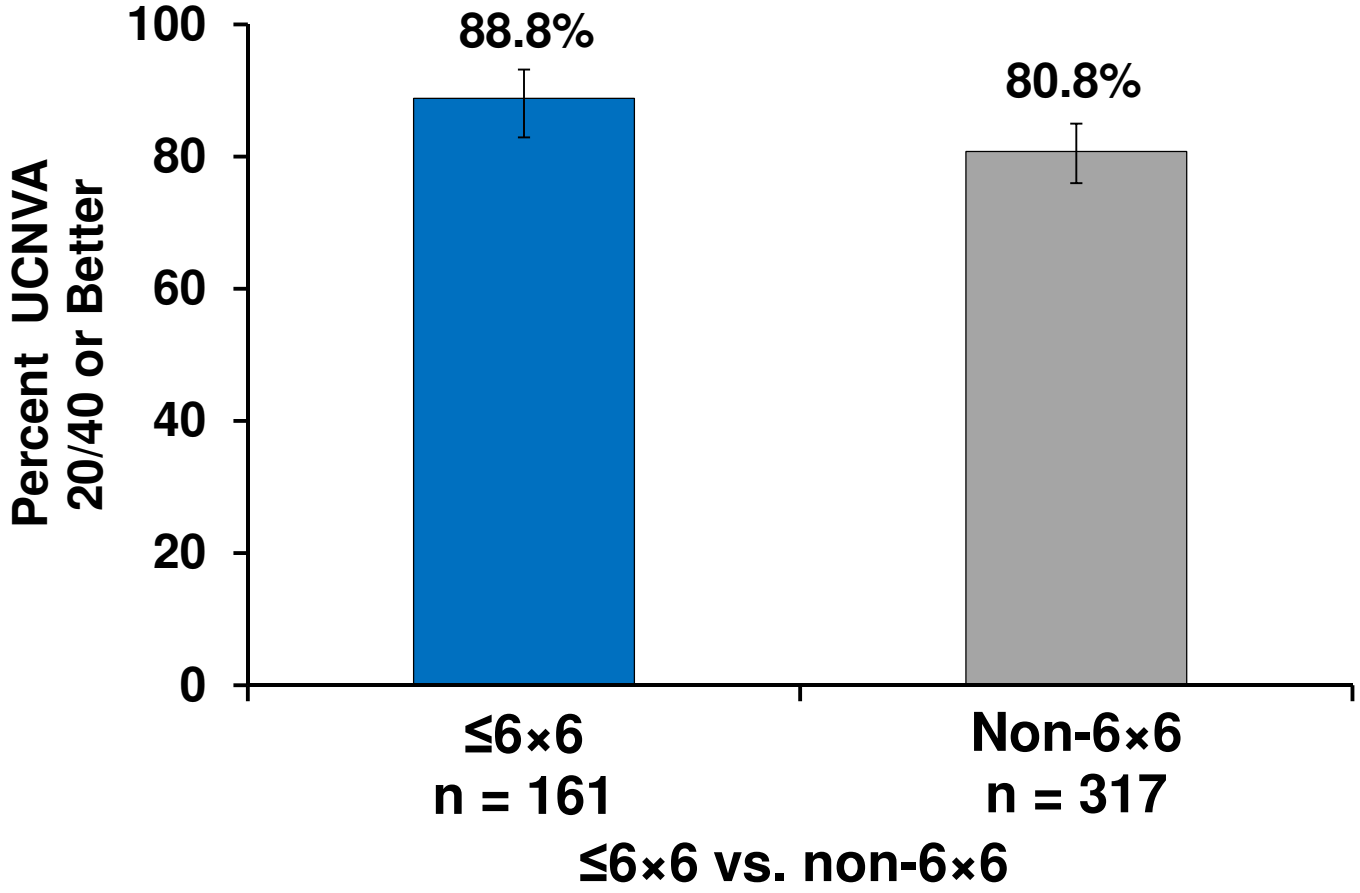
Mean UCNVA (SD):	36.7 (8.5)	40.4 (8.2)	43.4 (7.2)
Lines Improved (SD):	+3.3 (1.7)	+3.1 (1.6)	+2.7 (1.4)

Primary Effectiveness Endpoint at 12 Months Stratified by Preoperative Photopic Pupil Size



Mean UCNVA (SD):	40.1 (9.1)	41.0 (7.9)
Lines Improved (SD):	+2.8 (1.7)	+3.0 (1.5)

Primary Effectiveness Endpoint at 12 Months Stratified by ≤6×6 vs. Non-6×6



Mean UCNVA (SD):	42.0 (7.7)	40.1 (8.4)
Lines Improved (SD):	+3.1 (1.5)	+2.9 (1.6)

Secondary Effectiveness

Secondary Effectiveness Endpoint

- **Subjective improvement in near vision as measured by subject satisfaction questionnaire.**

How much has your need for reading glasses been **reduced in good lighting**?

1 = Not Reduced **7 = Very Reduced**

1	2	3	4	5	6	7

How much has your need for reading glasses been **reduced in dim lighting**?

1 = Not Reduced **7 = Very Reduced**

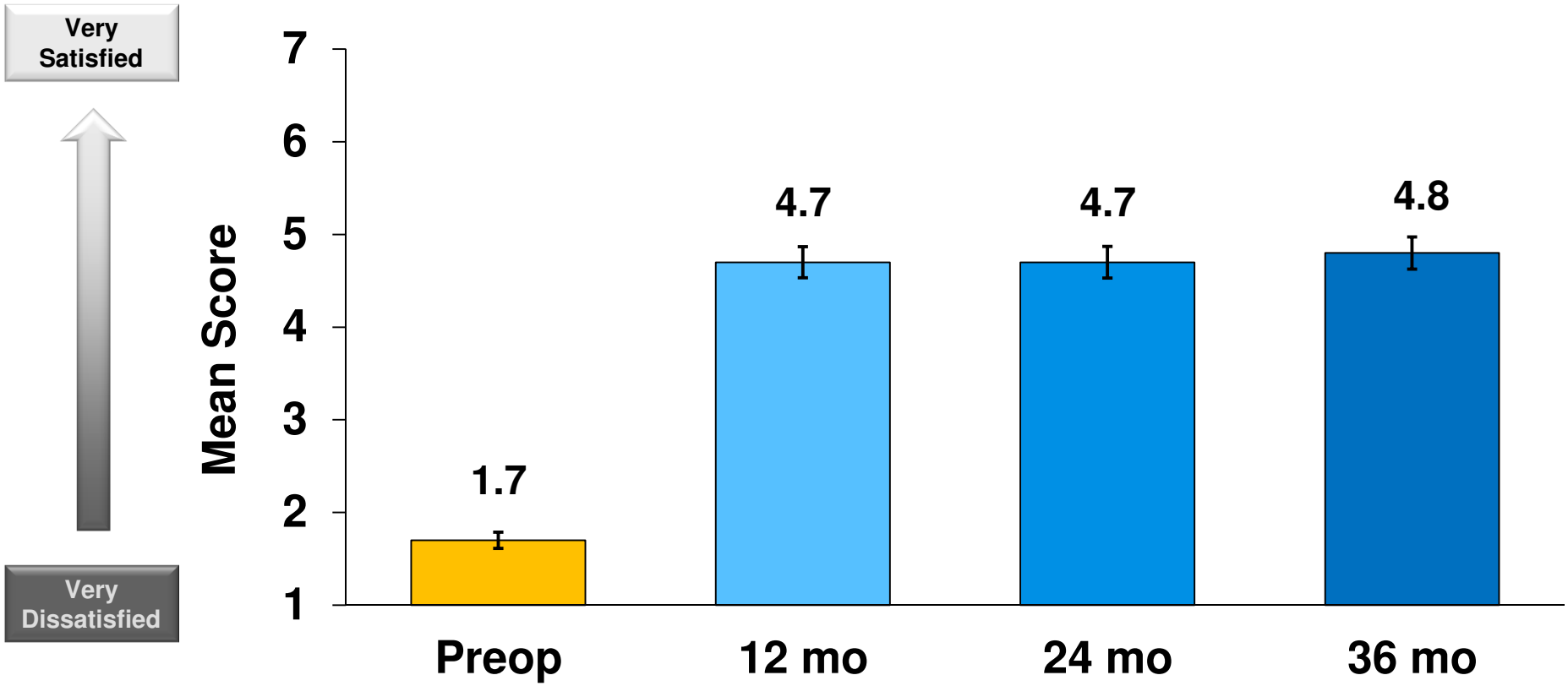
1	2	3	4	5	6	7

How **satisfied** are you with your near vision without reading glasses?

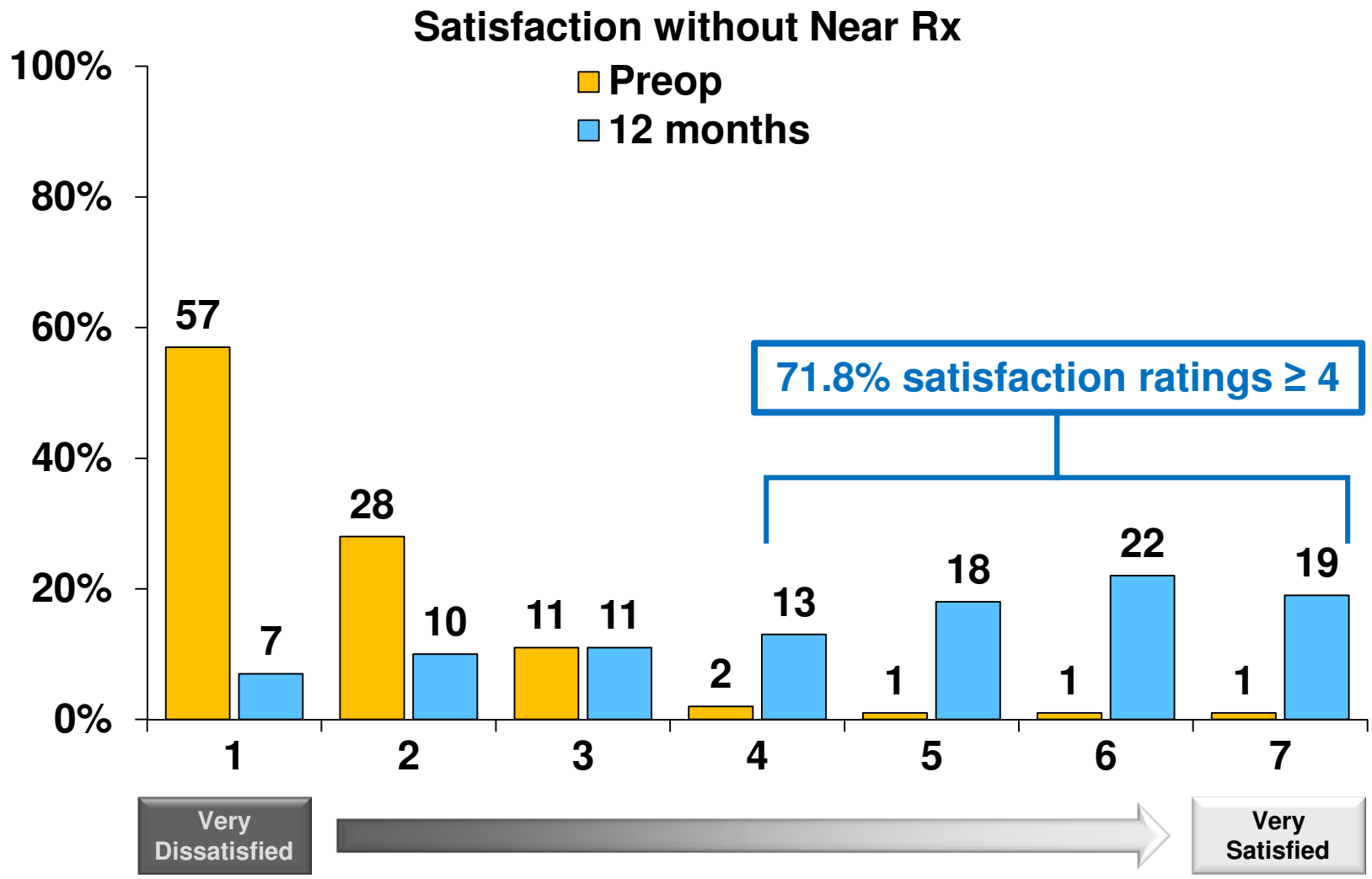
1 = Very Dissatisfied **7 = Very Satisfied**

1	2	3	4	5	6	7

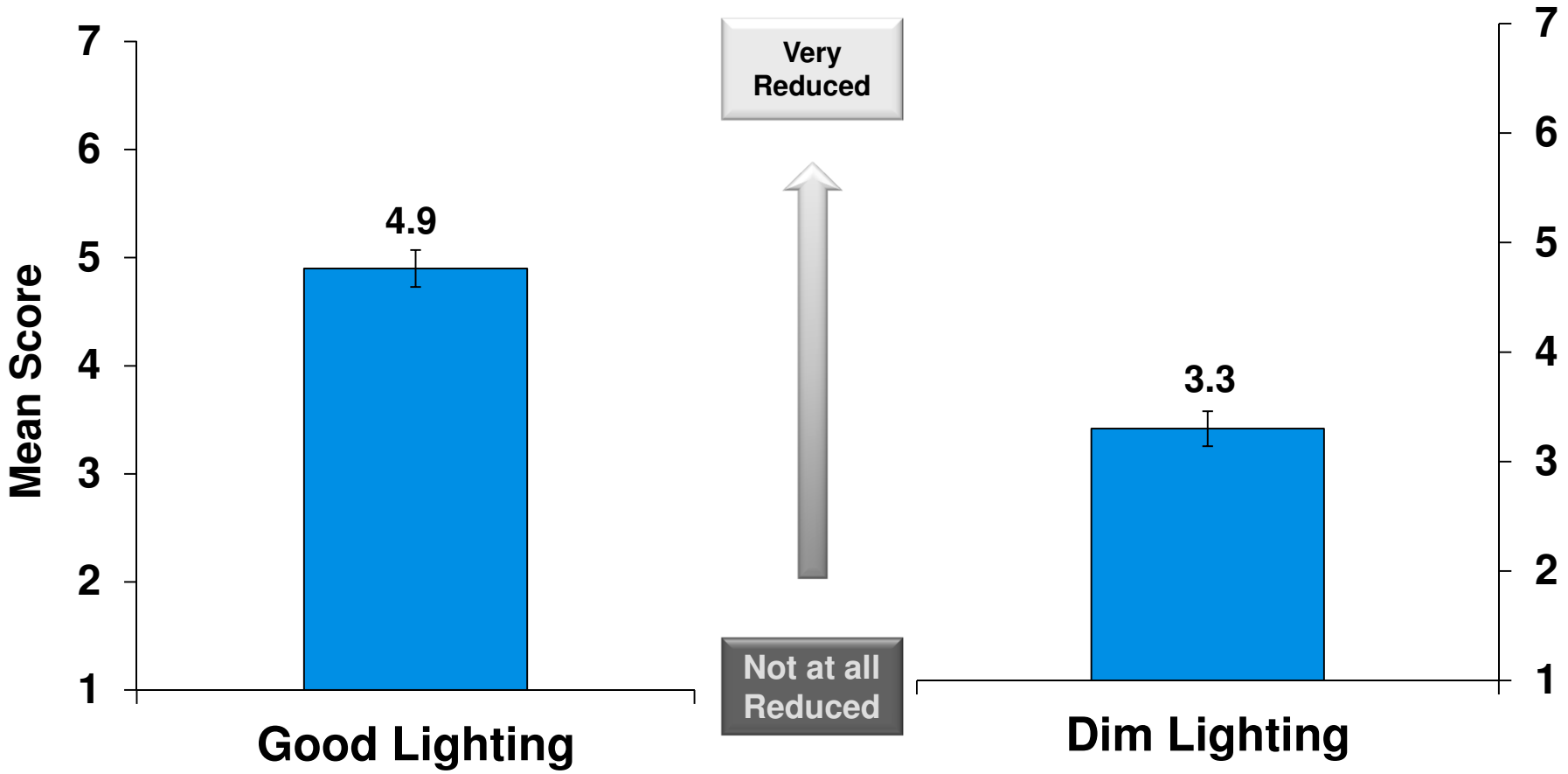
Satisfaction with Near Vision without Near Rx



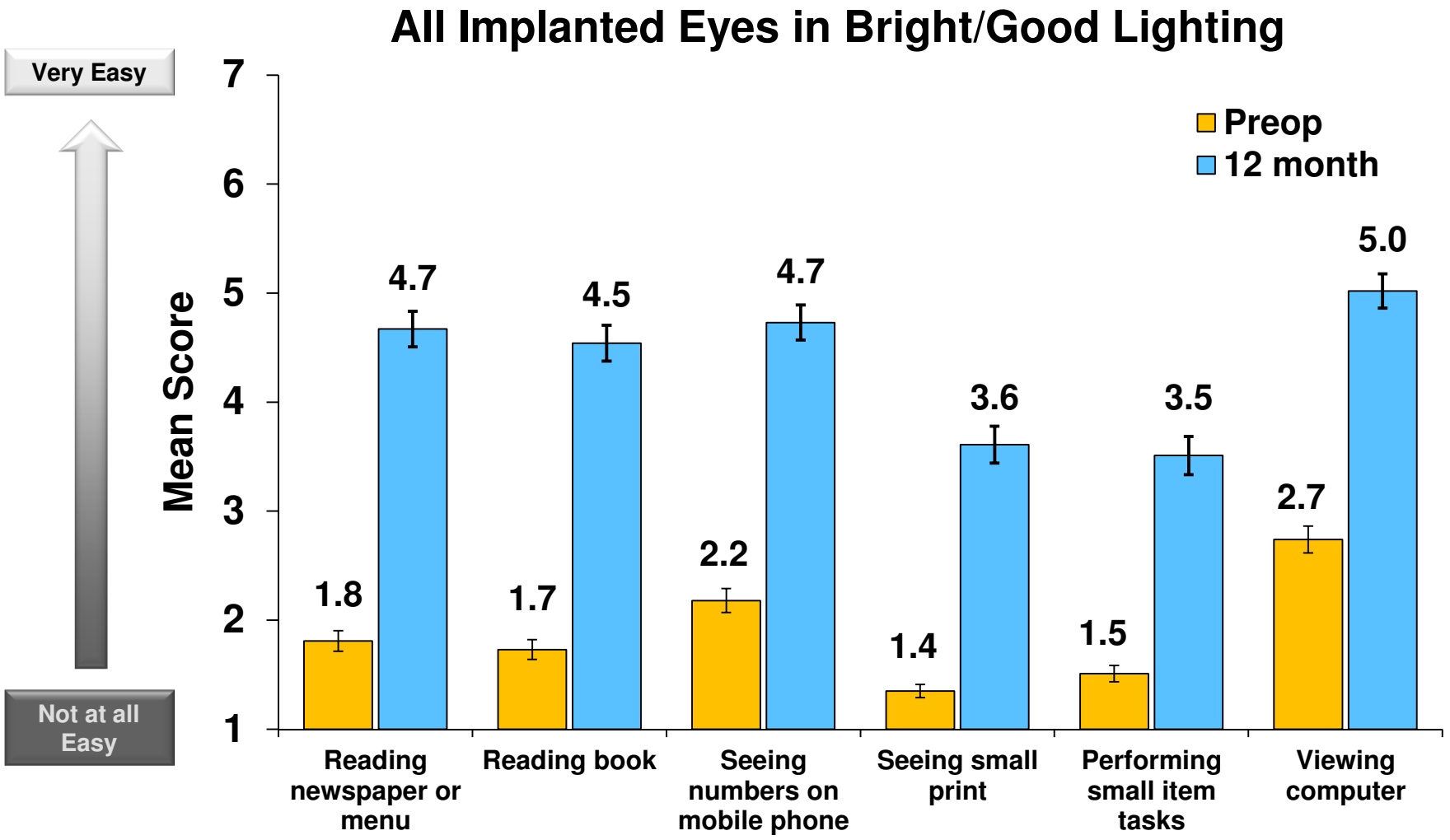
Satisfaction with Near Vision without Near Rx at 12 months



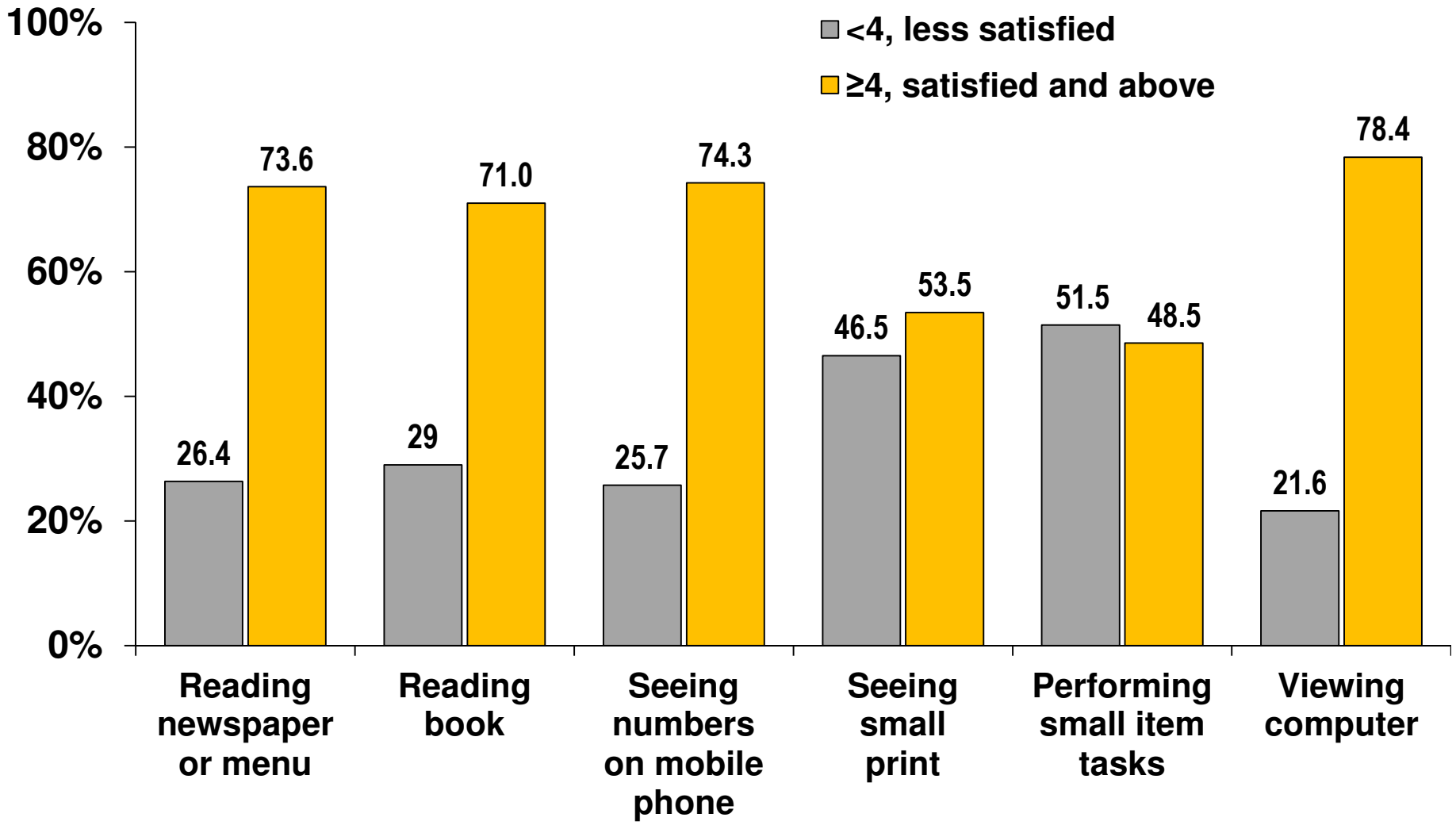
Reduction of Reading Glasses: 12 Months



Ease of Near and Intermediate Vision Tasks in Bright/Good Lighting at 12 Months

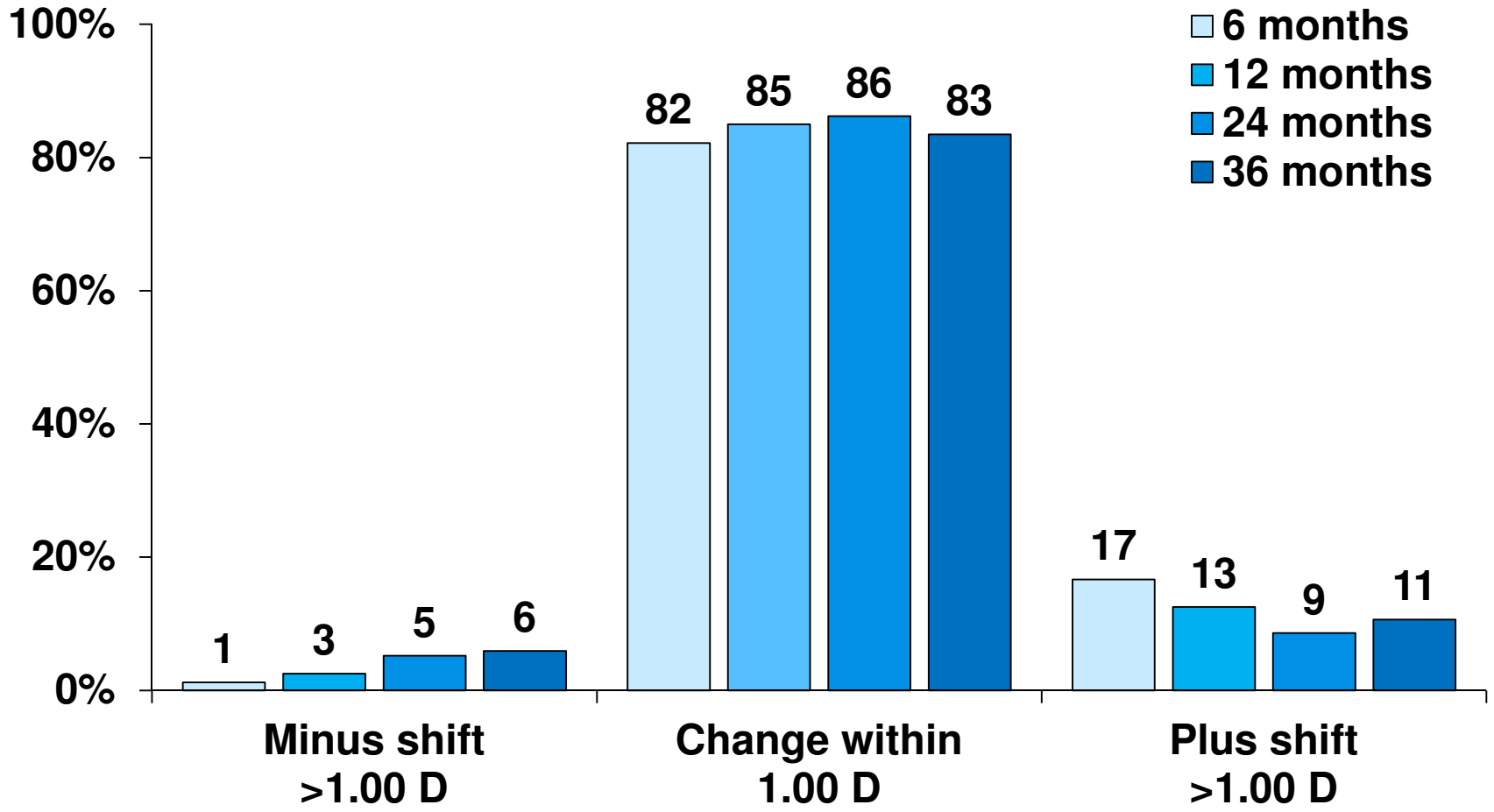


Distribution of Near/Intermediate Vision Task Ratings in Bright/Good Lighting at 12 Months

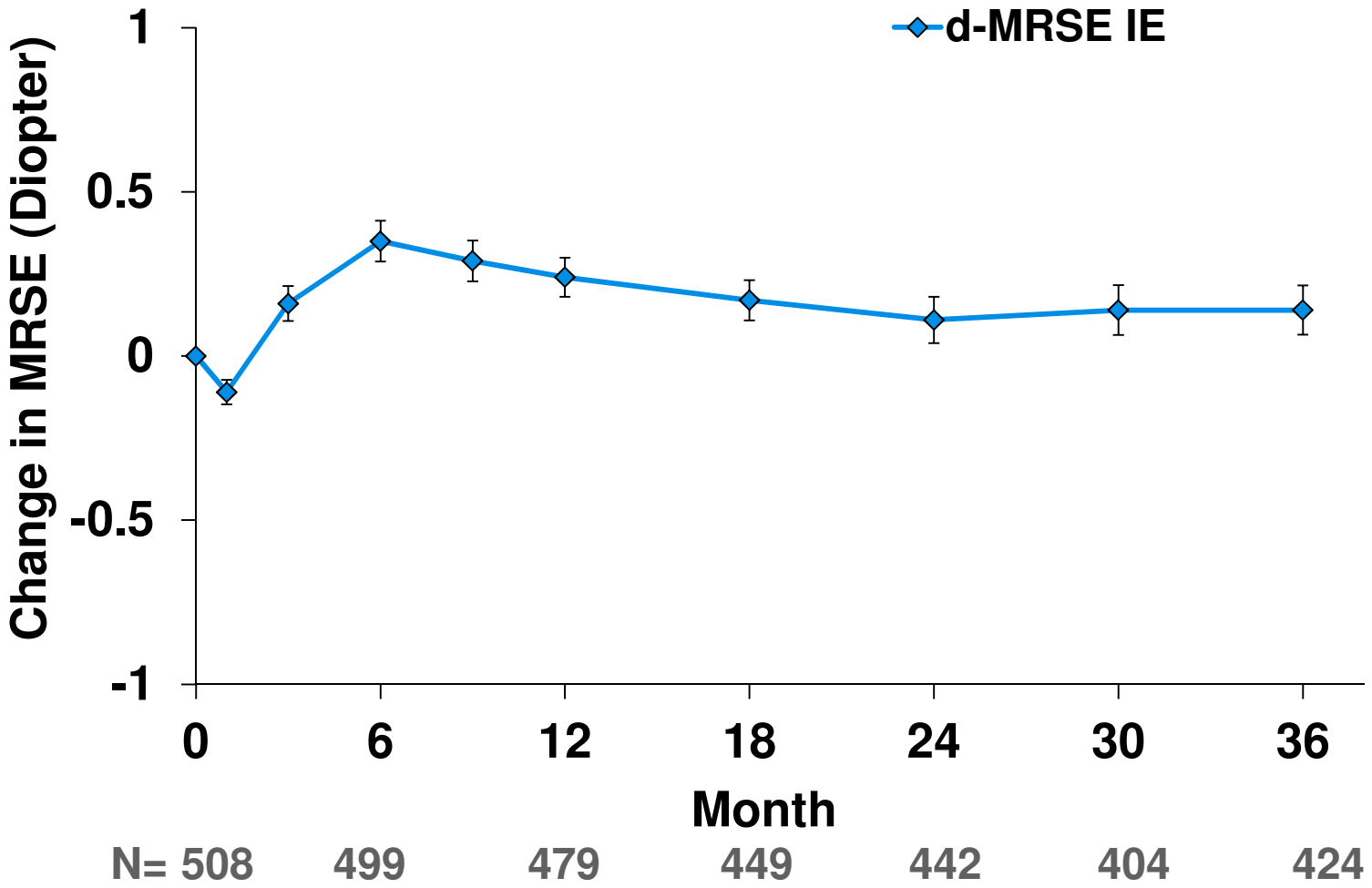


Refractive Stability

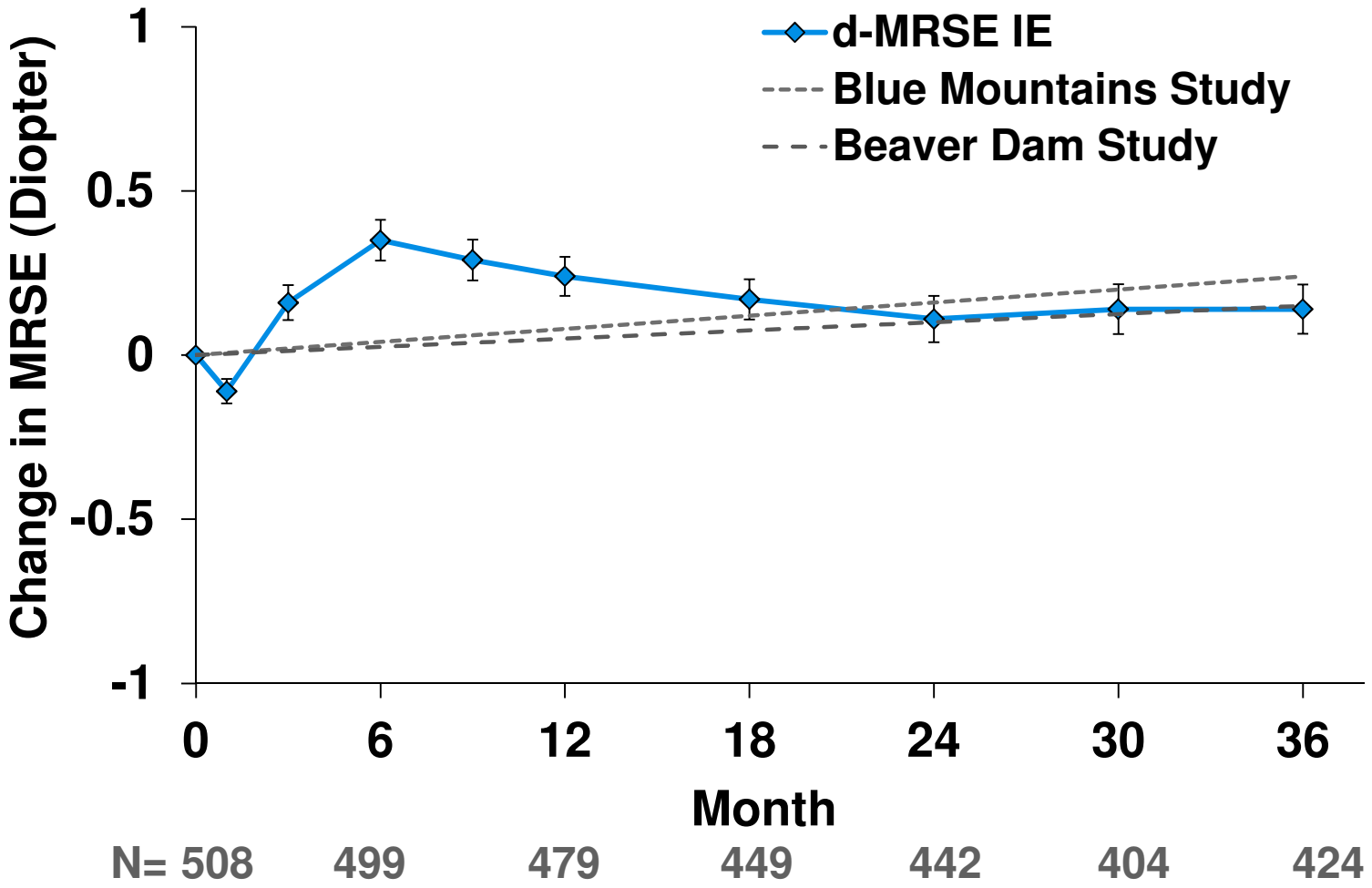
Distribution of Change in MRSE from Baseline



Change in MRSE from Baseline: Full Cohort

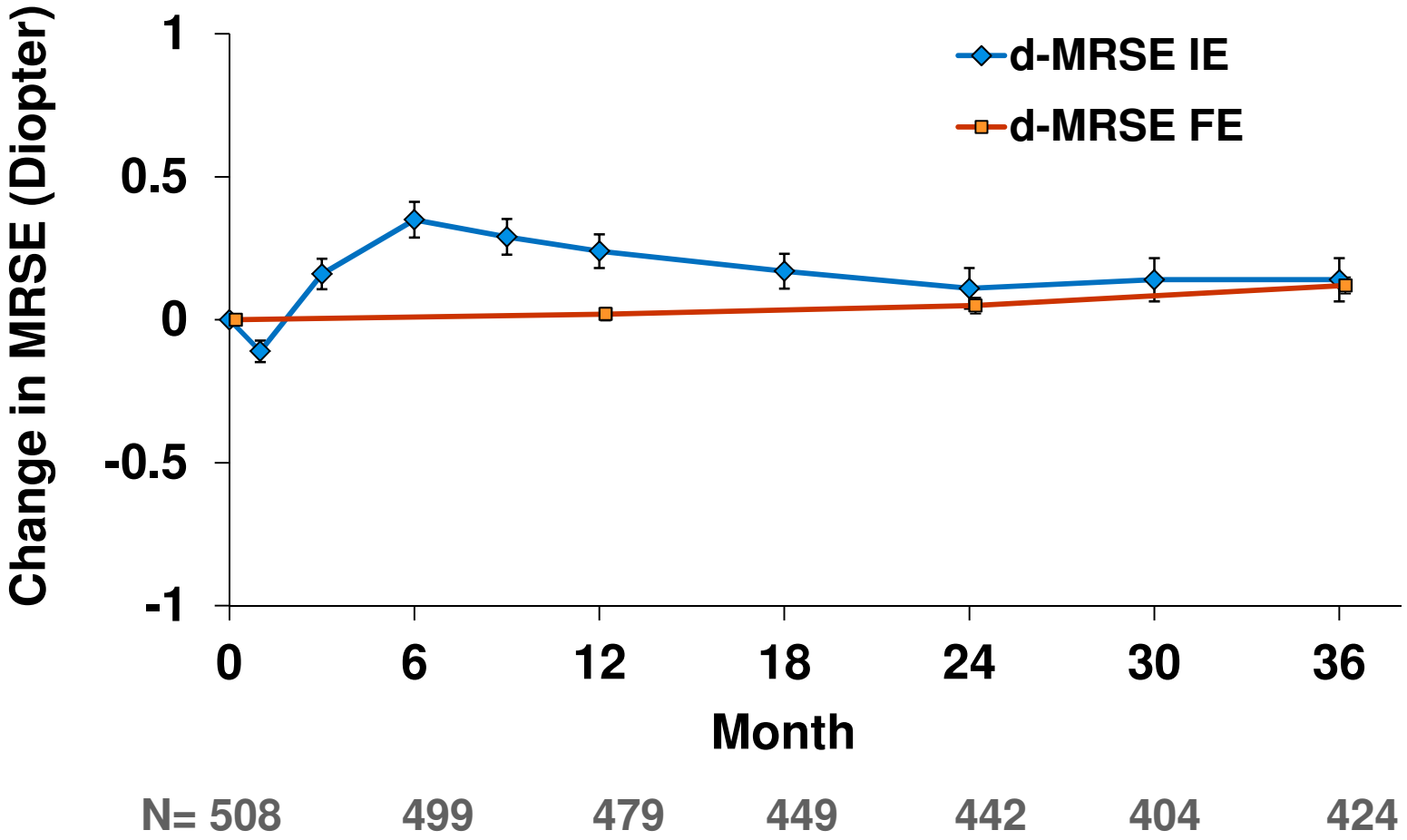


Change in MRSE from Baseline: Full Cohort



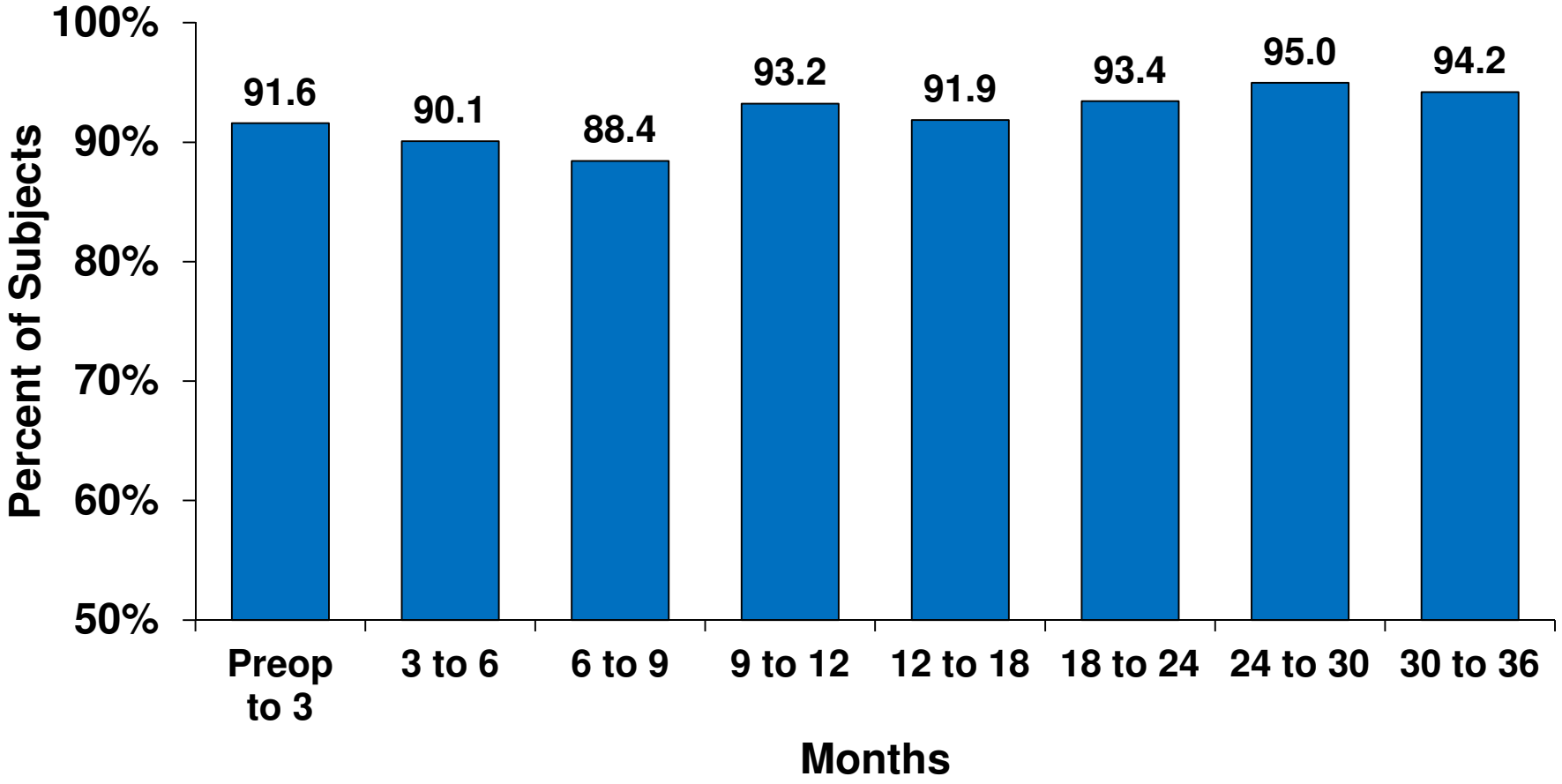
Analysis not previously submitted to FDA

Change in MRSE: Full Cohort

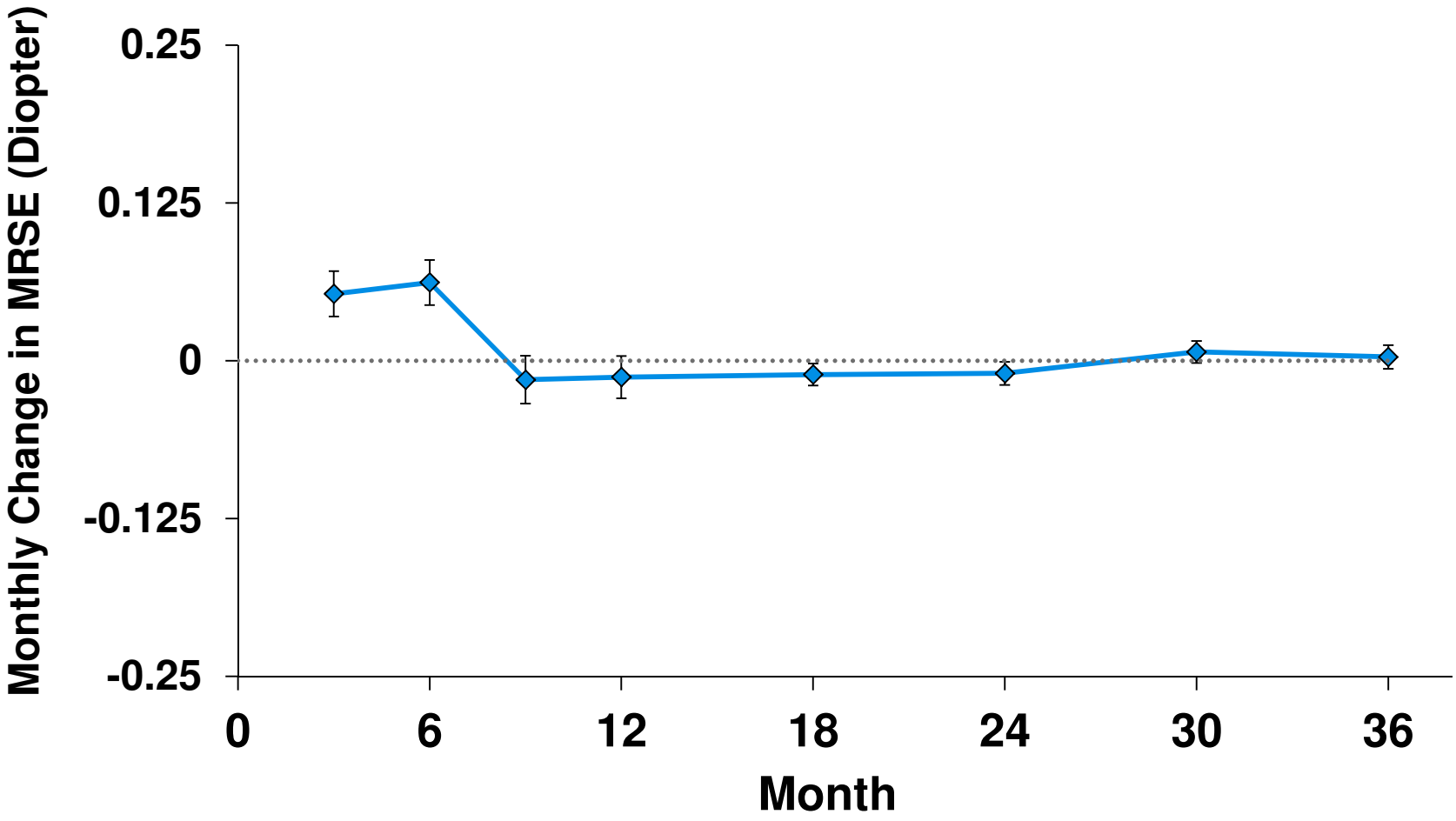


Analysis not previously submitted to FDA

≤1.00 D Change in MRSE Between Consecutive Visits



Monthly Change in MRSE Between Paired Sequential Visits



Determination of Refractive Stability

- ≥95% of eyes have a change of ≤1.00 D of MRSE between two refractions performed at least 3 months apart
- Mean rate of change in MRSE, as determined by paired analysis, ≤0.5 D per year (0.04 D/month) over the same time period
- Mean rate of change of MRSE decreases monotonically over time, with a projected asymptote of zero or a rate of change attributable to normal aging
- 95% CI for the mean rate of change includes zero or a rate of change attributable to normal aging

Refractive Stability

Criteria	Month-to-month interval when target was met:					
	6-9	9-12	12-18	18-24	24-30	30-36
≤1.00 D MRSE change between 2 consecutive visits					●	94.2%
≤0.50 D per year (0.04 D/month) mean rate of change in MRSE	●	●	●	●	●	●
95% CI for the mean rate of change includes zero	●	●			●	●
Mean rate of change of MRSE over time, approaching zero (or a rate of change attributable to normal aging)					●	●

Summary of Effectiveness

- Data provides reasonable assurance that KAMRA inlay is effective in improving UCNVA
  - Consistent improvement in near vision by increasing depth of focus, while maintaining distance vision
- Results are sustained through 3 years of study
- Improves satisfaction with near/intermediate vision and tasks

Presentation Agenda

Introduction	**Nick Tarantino, OD** *Chief Clinical & Regulatory Officer* *AcuFocus, Inc.*
Clinical Landscape	**Vance Thompson, MD** *Clinical Investigator*
Study Design	**Corina van de Pol, OD, PhD** *VP Clinical Research* *AcuFocus, Inc.*
Effectiveness	**John A Vukich, MD** *Clinical Investigator*
Safety	**Jay Pepose, MD, PhD** *Clinical Investigator*
Optimization of Surgical Procedure	**Dan Durrie, MD** *Clinical Investigator*
Benefit/Risk Conclusions	**John A Vukich, MD** *Clinical Investigator*

Safety Results

Jay S. Pepose, MD, PhD

Clinical Investigator

Professor of Clinical Ophthalmology

Washington University School of Medicine
Director, Pepose Vision Institute

St. Louis, Missouri

Safety

- **Primary Safety Endpoints**
  - **BCDVA loss, induced astigmatism, and slit lamp findings of stromal haze**
  - **Adverse Events (AEs)**
- **Intraocular Pressure**
- **Contrast Sensitivity**
- **Patient Reported Symptoms**
- **Endothelial Cell Density**

Primary Safety Endpoints: 12 Months

- **Preservation of best spectacle-corrected visual acuity**
  - **<5% of eyes with a *persistent* loss of 2 or more lines of BCDVA**
  - **<1% of eyes with BCDVA worse than 20/40 (for those eyes with preop BCDVA of 20/20 or better)**
- **Induced manifest refractive astigmatism**
  - **≤5% of eyes with more than 2.00 D of induced refractive astigmatism**
- **Clinically significant haze on slit lamp evaluation**
  - **<1% of eyes with clinically significant haze associated with BCDVA loss >2 lines**
- **Cumulative incidence of device-related ocular AEs**
  - **<5% of eyes with device-related AEs and <1% occurrence rate for any single device-related AE**

Summary of Safety Endpoints at 12 months

Safety Parameters at 12 months	n/N (%) (All available eyes)
<5% with persistent BCDVA loss ≥2 lines at two consecutive visits	3/479 (0.6%)
<1% with BCDVA worse than 20/40 if 20/20 or better preoperatively	0/479 (0%)
<1% with ≥ trace corneal haze in conjunction with loss of BCDVA >2 lines	0/479 (0%)
<5% with induced refractive astigmatism >2.0 D (not due to irregular astigmatism)	0/479 (0%)

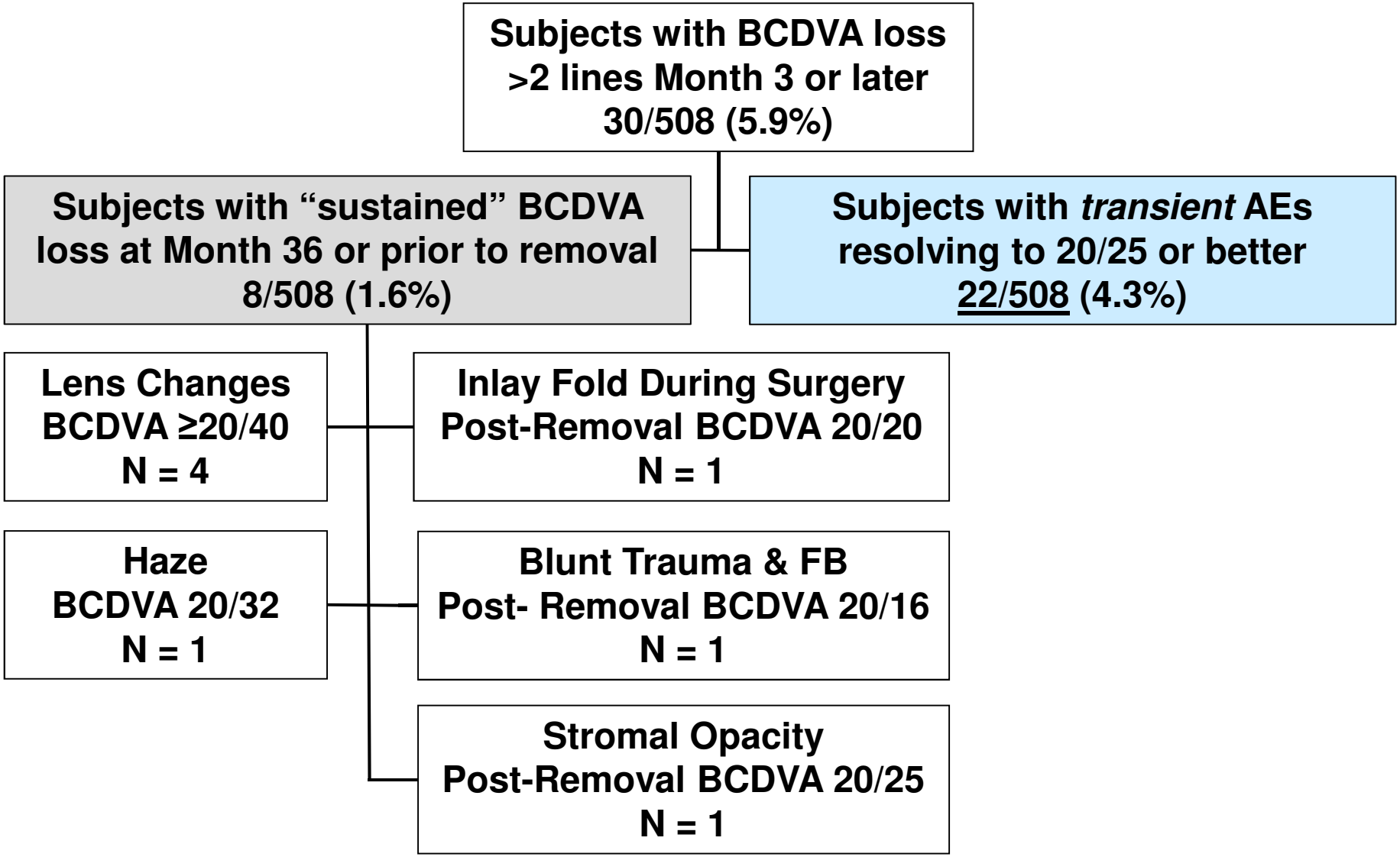
Cumulative Incidence of Ocular AEs ≥1%

Category	Adverse Event	Number of Events	Subjects, n (%) N = 508
Cornea	Conjunctivitis	11	10 (2.0)
Flap Complication	DLK	6	6 (1.2)
IOP	IOP Increase >10 mmHg above baseline or >25 mmHg with clinical findings	27	17 (3.3)
Secondary Surgical Intervention	Re-centration	6	6 (1.2)
	Removals	44	44 (8.7)
Vision	Decrease in BCDVA >2 lines at Month 3 or later	36	30 (5.9)

Incidence of Ocular AEs ≥1% (N = 508)

Category	Adverse Event	# of Subjects n (%) 12M	Additional # of Subjects n (%) 12-24M	Additional # of Subjects n (%) 24-36M
Cornea	Conjunctivitis	5 (1.0)	2 (0.4)	3 (0.6)
Flap Complication	DLK	6 (1.2)	0 (0.0)	0 (0.0)
IOP	IOP Increase >10 mmHg above baseline or >25 mmHg with clinical findings	15 (3.0)	1 (0.2)	1 (0.2)
SSI	Re-centration	1 (0.2)	5 (1.0)	0 (0.0)
	Removals	15 (3.0)	21 (4.1)	8 (1.6)
Vision	Decrease in BCDVA >2 lines at Month 3 or later	17 (3.3)	11 (2.2)	2 (0.4)

Cumulative Adverse Events: BCDVA Loss >2 Lines Month 3 or Later



Cumulative Removals

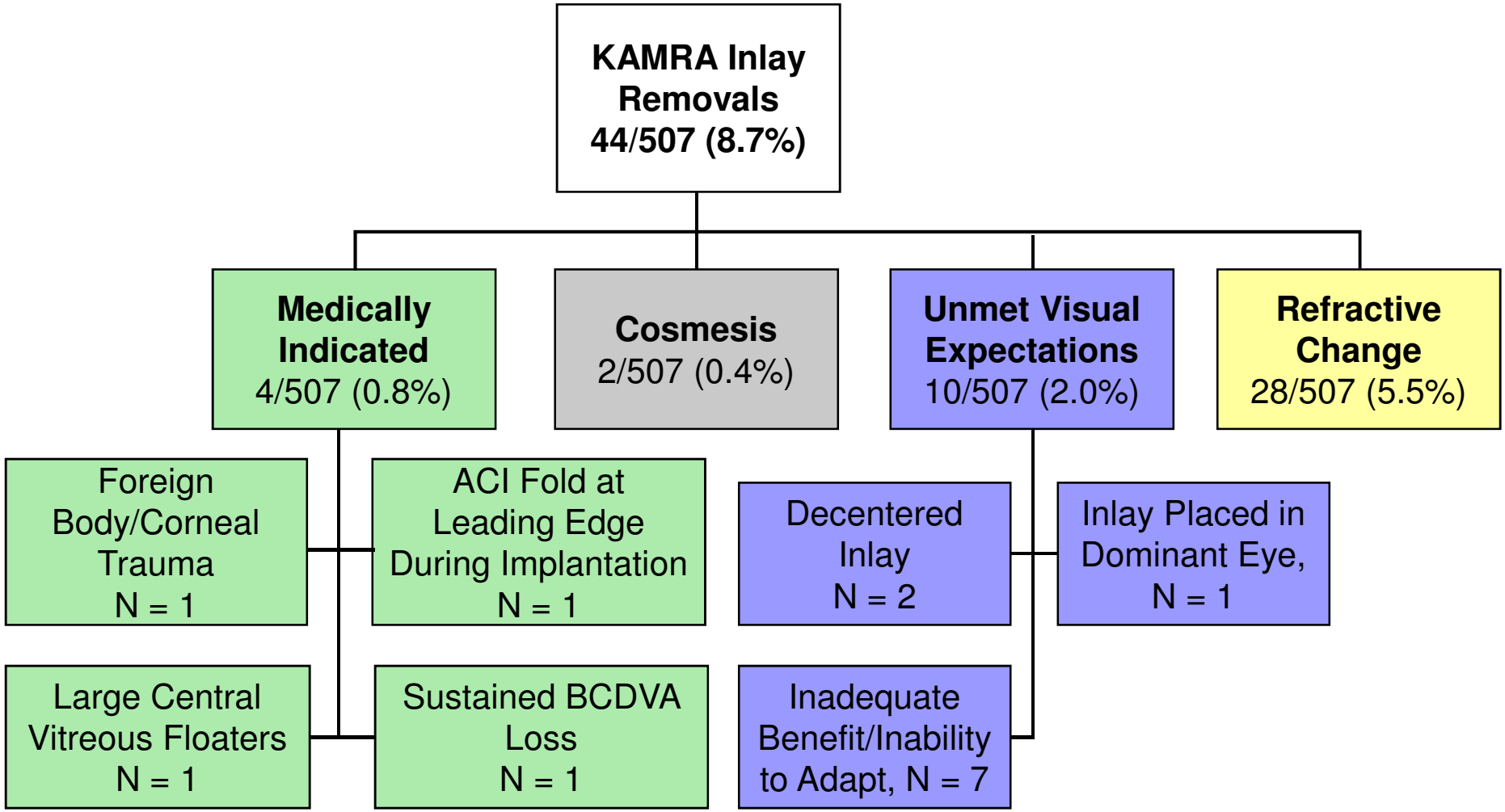
- **44 total removals (8.7%) –**
  - **4 (0.8%) medically-indicated removals**
  - **2 (0.4%) removals related to cosmesis**
  - **10 (2.0%) unmet visual expectations**

  BCDVA recovered to within 1 line of baseline

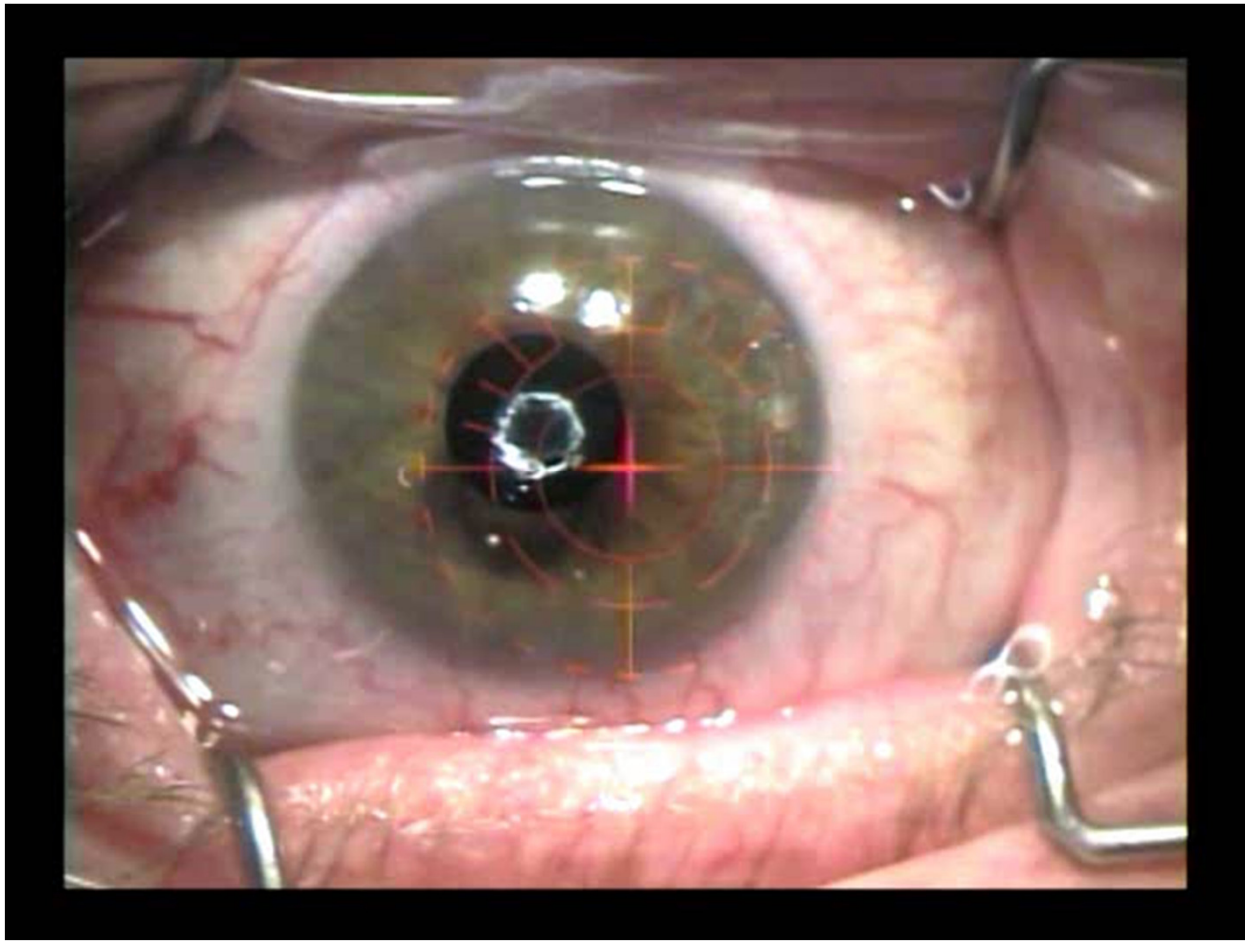
  - **28 (5.5%) refractive change**

  Discussed in next section

KAMRA™ Inlay Removals



Video of Removal Procedure



- Post-removal visits at 1 day, 1 week, 1 month, 3 months, and 6 months and longer as required

Post-Removal BCDVA: All Removals

	Last Available Post-removal (N = 44)
Mean letters ± SD	53.0 (20/16) ± 2.6
Range	43 (20/25) to 55 (20/16)
≥20/20 or better	43 (97.7%)
≥20/25 or better	44 (100.0%)

	Change in BCDVA
Mean letters ± SD	-0.9 ± 2.4
Range	-7 to +4

Post-Removal MRSE: All Removals

	Last Available Post-removal (N=44)
Mean MRSE (SD)	+0.48 D (0.86)
Range	-0.5 D to +4.25 D

	Change in MRSE
Mean Change MRSE from Baseline (SD)	+0.37 D (0.77)
Range	-1.0 D to +4.0 D

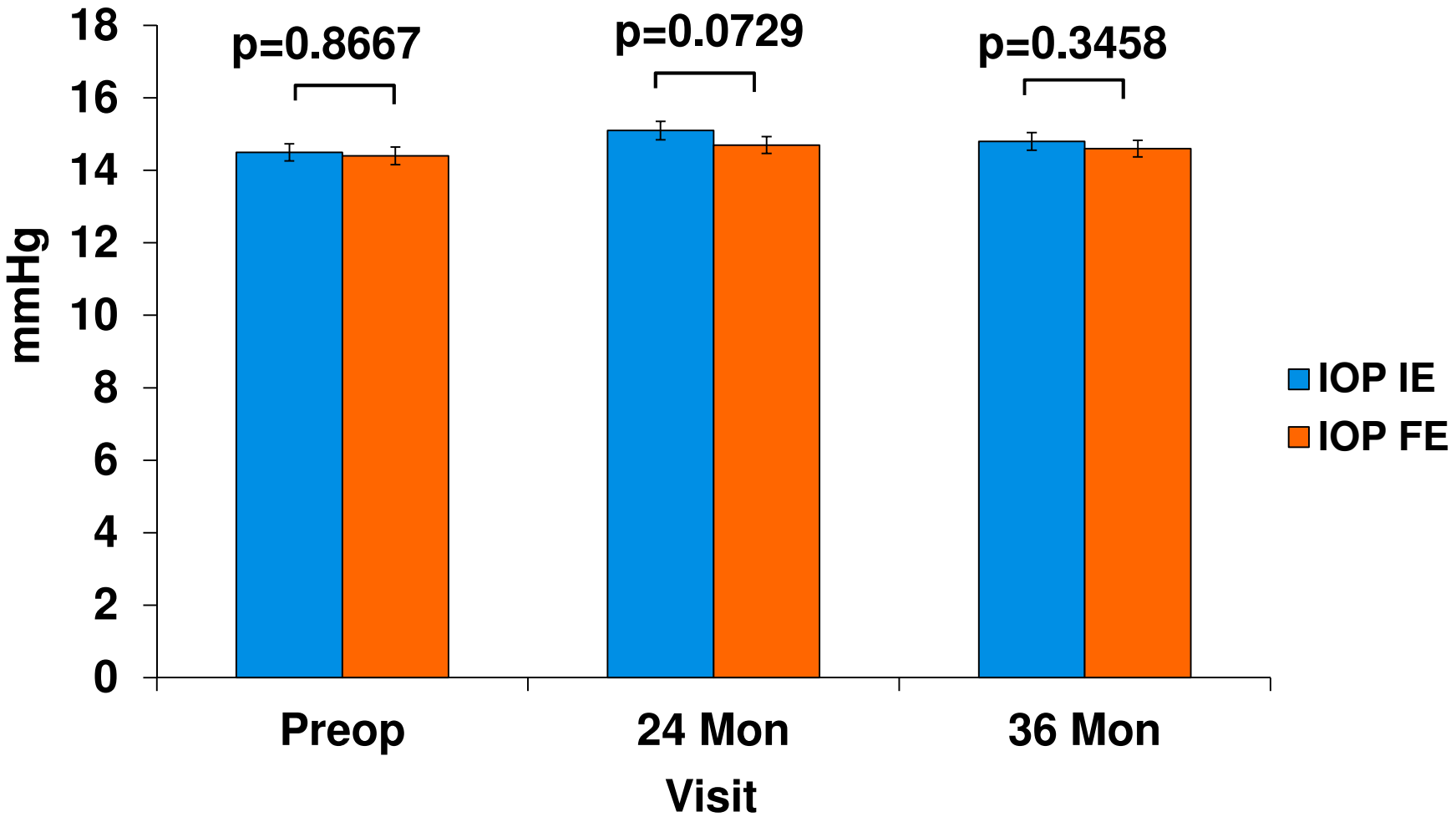
Safety

- Primary Safety Parameters
  - BCDVA loss, induced astigmatism, and slit lamp findings of stromal haze
  - Adverse Events (AEs)
- **Intraocular Pressure**
- Contrast Sensitivity
- Patient Reported Symptoms
- Endothelial Cell Density

Adverse Event: Elevated IOP

- IOP increase >10 mmHg above baseline or IOP >25 mmHg
  - 17 (3.3%) subjects experienced steroid-related IOP increases [IOP range: 20-44]
  - All IOP AEs resolved with no subjects remaining on IOP-lowering medications
  - IOP increases were not directly related to presence of inlay

Implant Eye vs. Fellow Eye IOP



Analysis not previously submitted to FDA

Safety

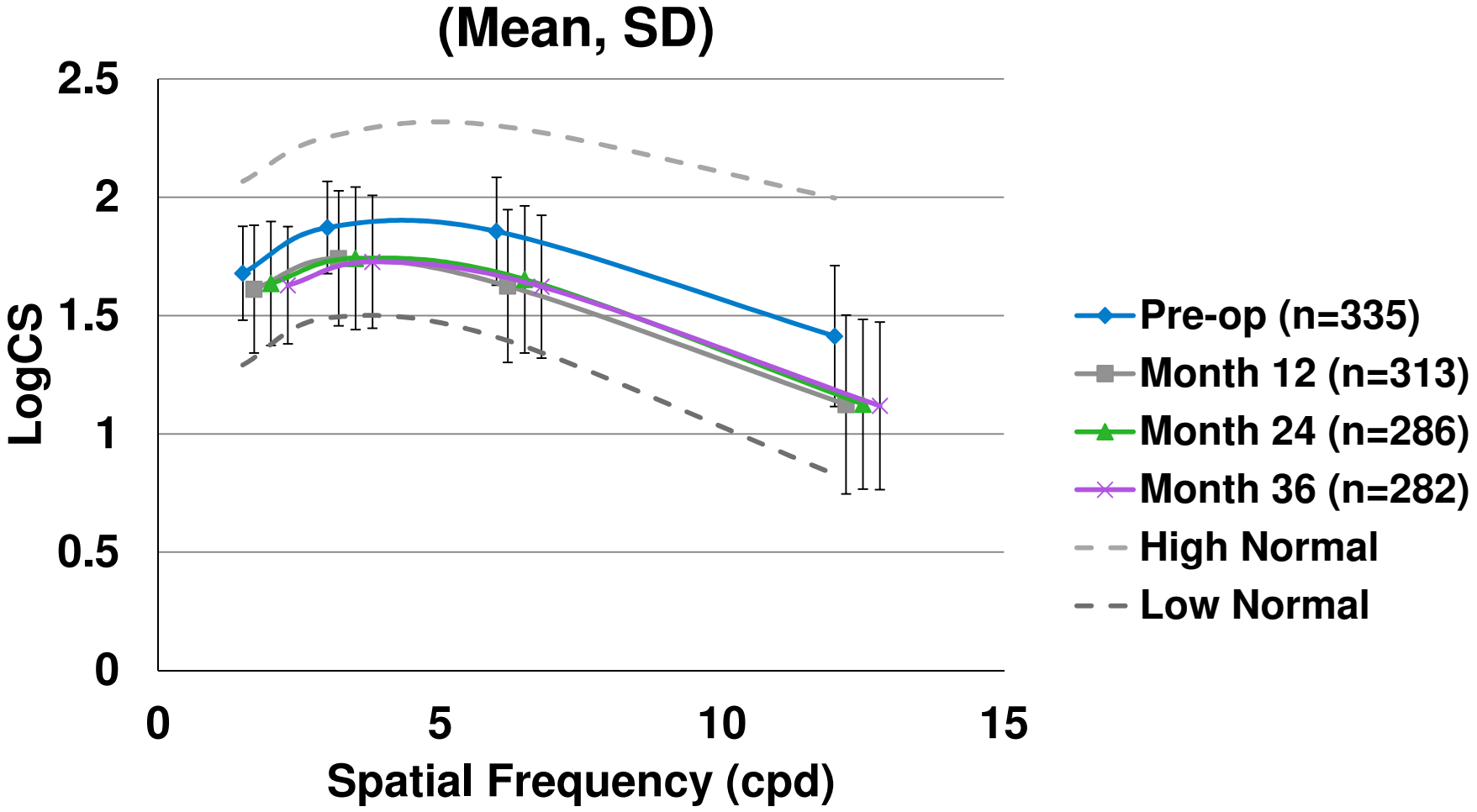
- Primary Safety Parameters
  - BCDVA loss, induced astigmatism, and slit lamp findings of stromal haze
  - Adverse Events (AEs)
- Intraocular Pressure
- **Contrast Sensitivity**
- Patient Reported Symptoms
- Endothelial Cell Density

Overview of Contrast Sensitivity (CS) Function

- Decrease in monocular CS function from baseline at all spatial frequencies, with mean postoperative CS function remaining stable and within normal ranges
  - "Normal" ranges defined as Preop Mean ± 1.96 standard deviations*
- No change in binocular CS function from baseline, with mean postoperative CS function remaining stable

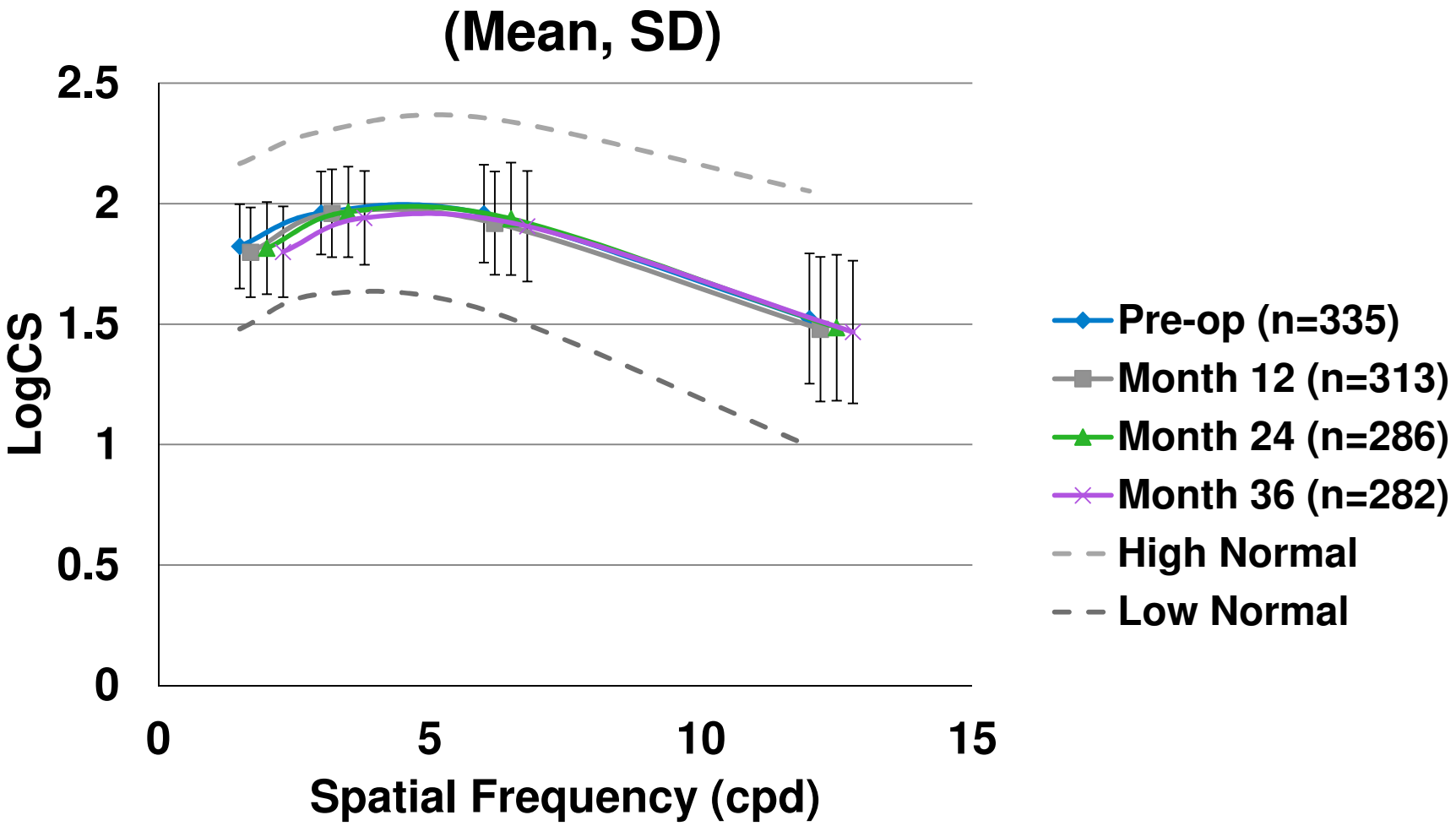
*Definition of normal range not submitted to by FDA

Monocular Mesopic CS Without Glare



Curves slightly offset for ease of comparison

Binocular Mesopic CS Without Glare



Curves slightly offset for ease of comparison

Safety

- Primary Safety Parameters
  - BCDVA loss, induced astigmatism, and slit lamp findings of stromal haze
  - Adverse Events (AEs)
- Intraocular Pressure
- Contrast Sensitivity
- **Patient Reported Symptoms**
- Endothelial Cell Density

Patient Reported Outcomes: Symptoms

Example questionnaire item for symptoms

Please mark (circle, X, or ✓ NO or YES) which, if any, of the following conditions you have experienced **using both eyes** in the past **4 weeks**. If you mark **YES**, please **rank the severity** of the condition. If you mark **NO**, **do not rank** the severity.

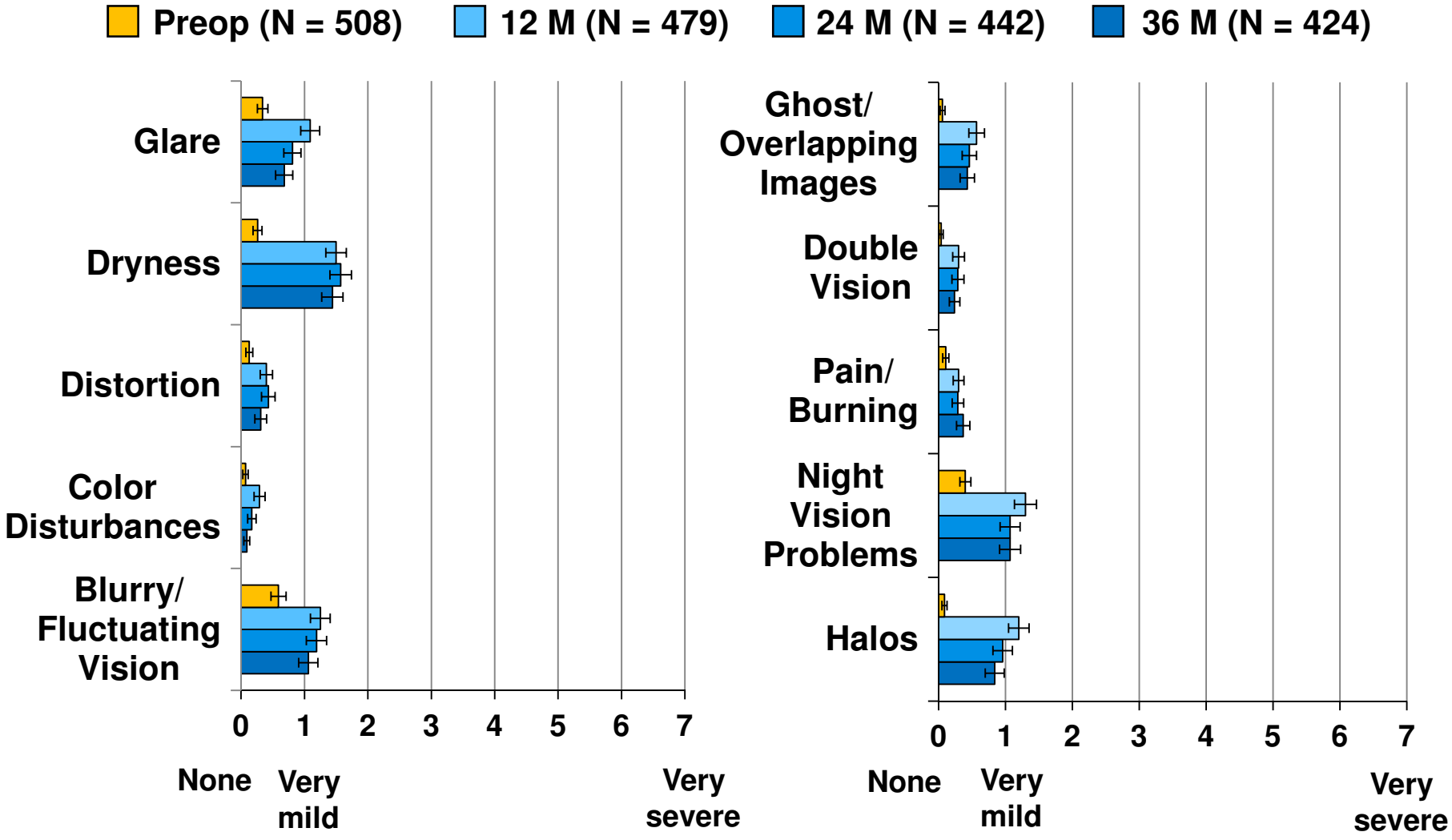
Blurry/Fluctuating Vision | No | Yes

If YES, please grade the severity.

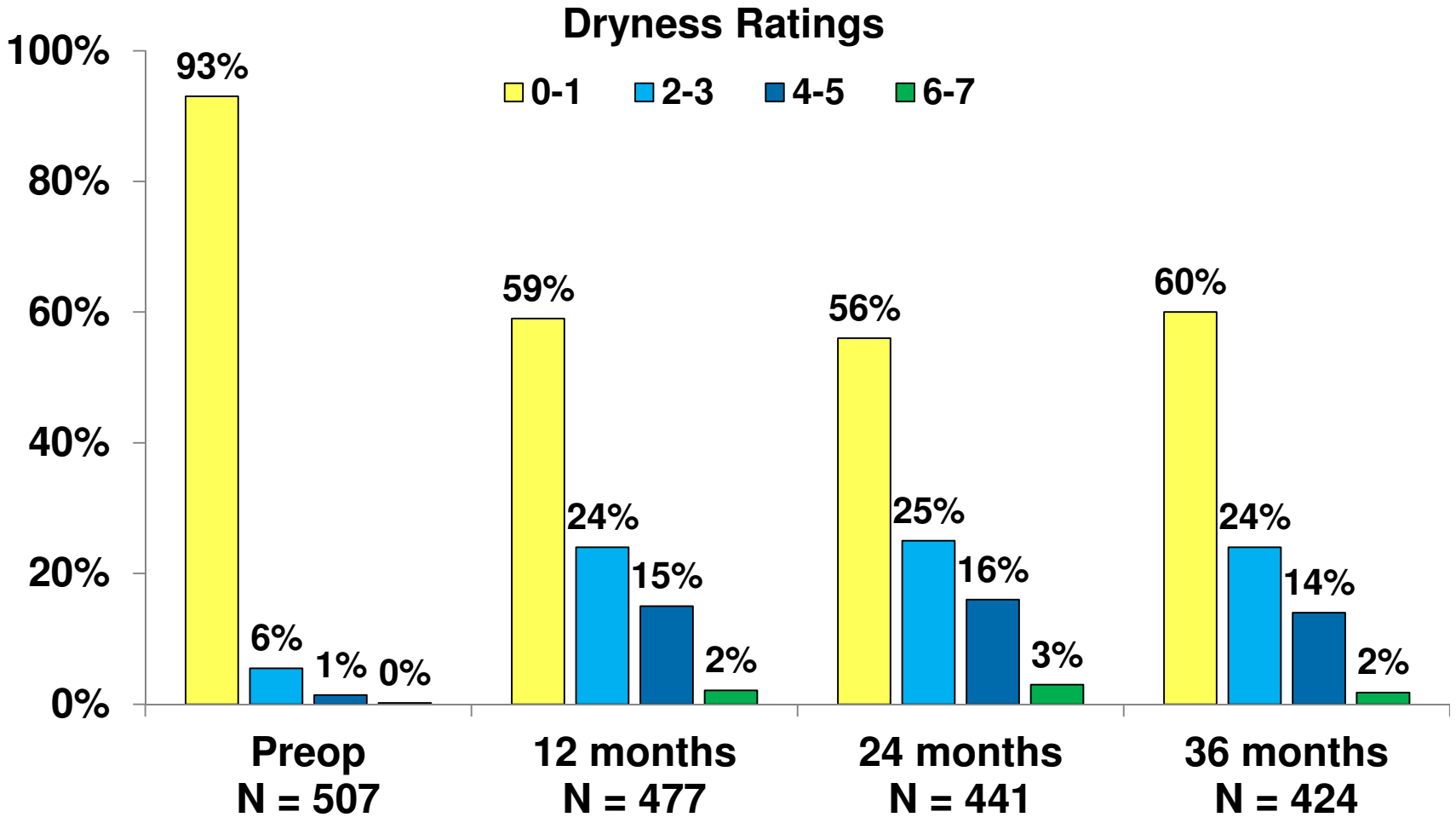
7 = Very Severe **1 = Very Mild**

7	6	5	4	3	2	1

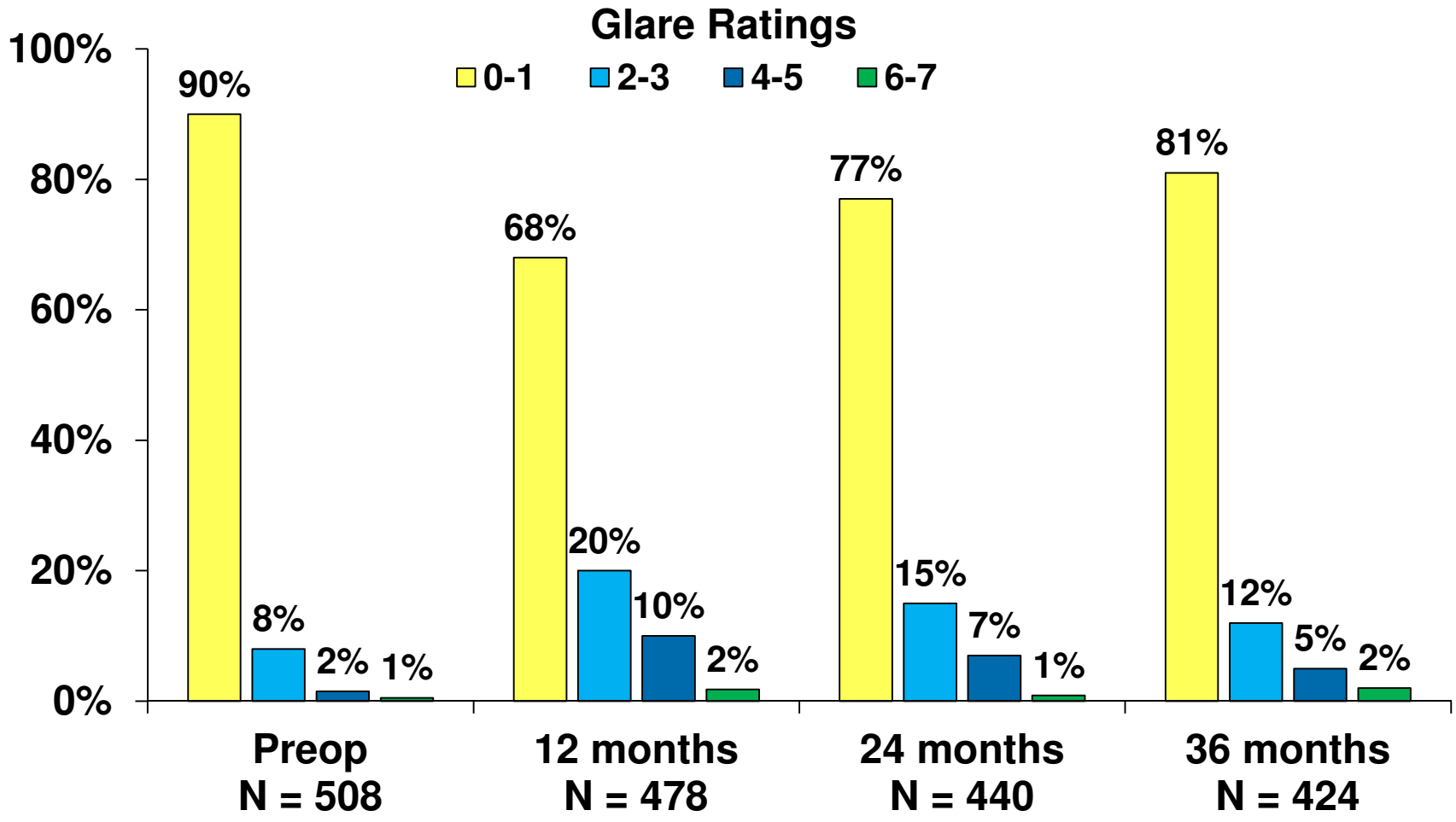
Symptoms Ratings at Preop,12, 24, & 36 Months (Safety Population)



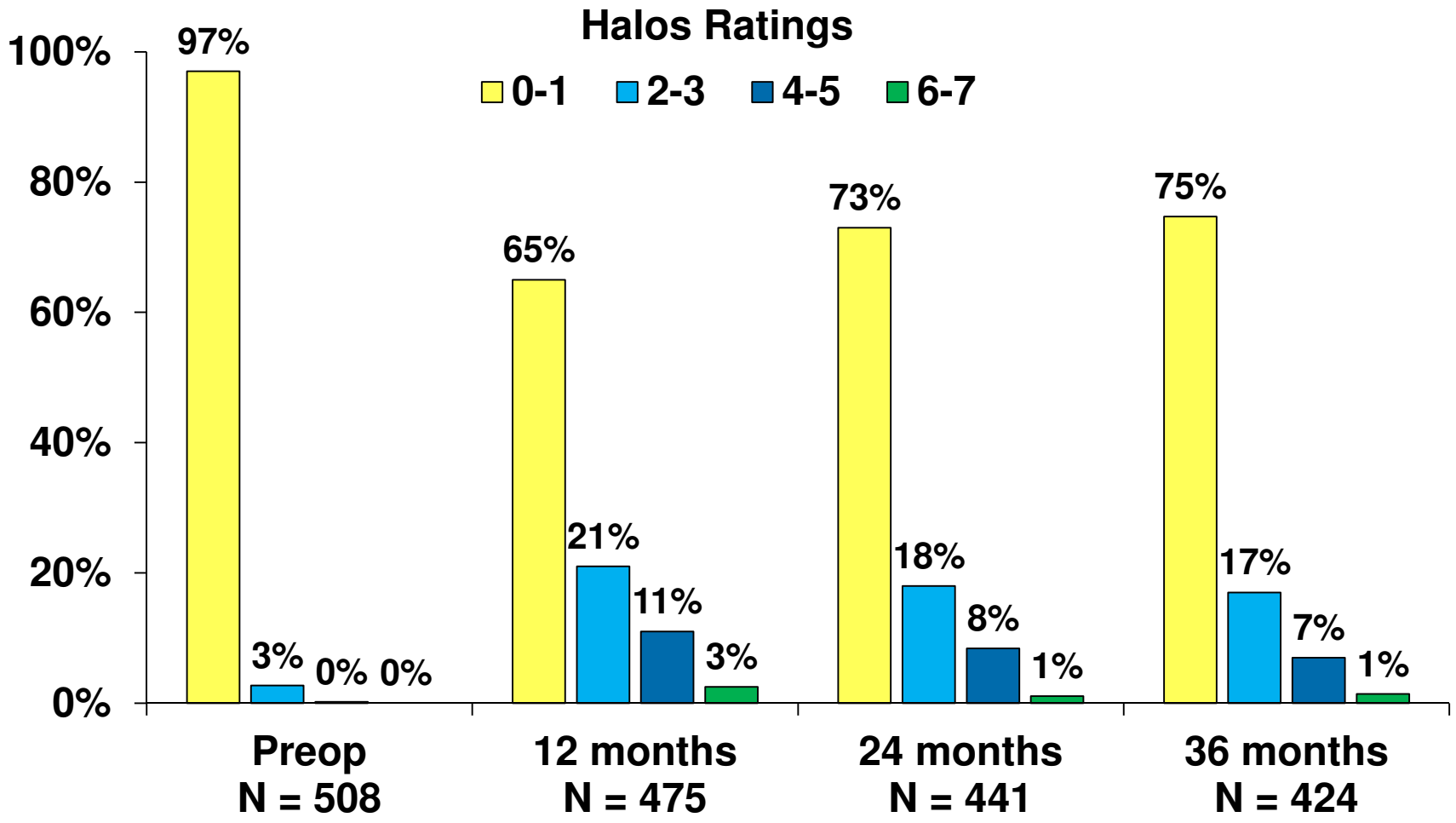
Distribution of Ratings: Dryness



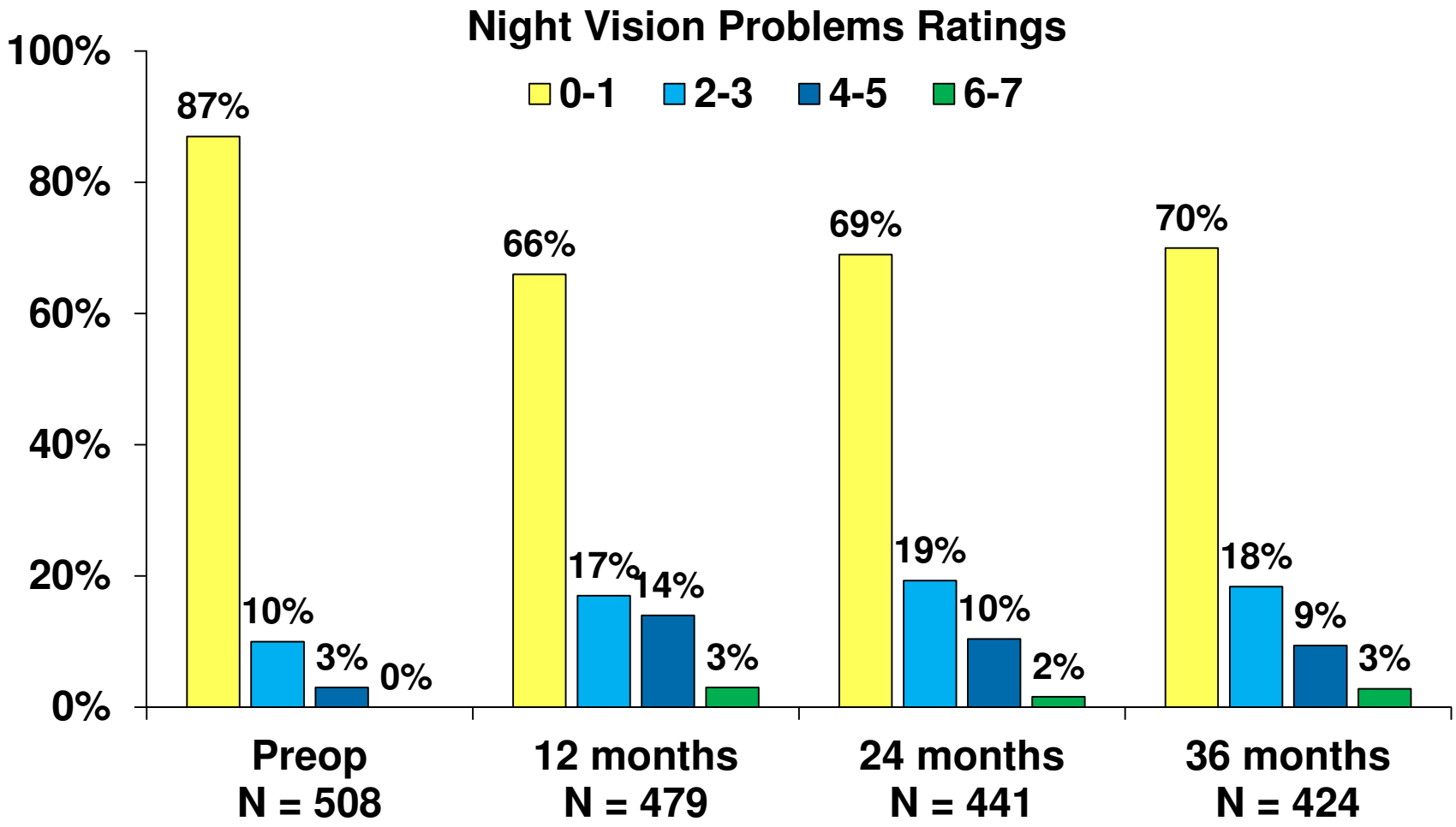
Distribution of Ratings: Glare



Distribution of Ratings: Halos



Distribution of Ratings: Night Vision Problems



Impact of Mesopic Pupil Size on Symptoms: Preoperative vs Month 12

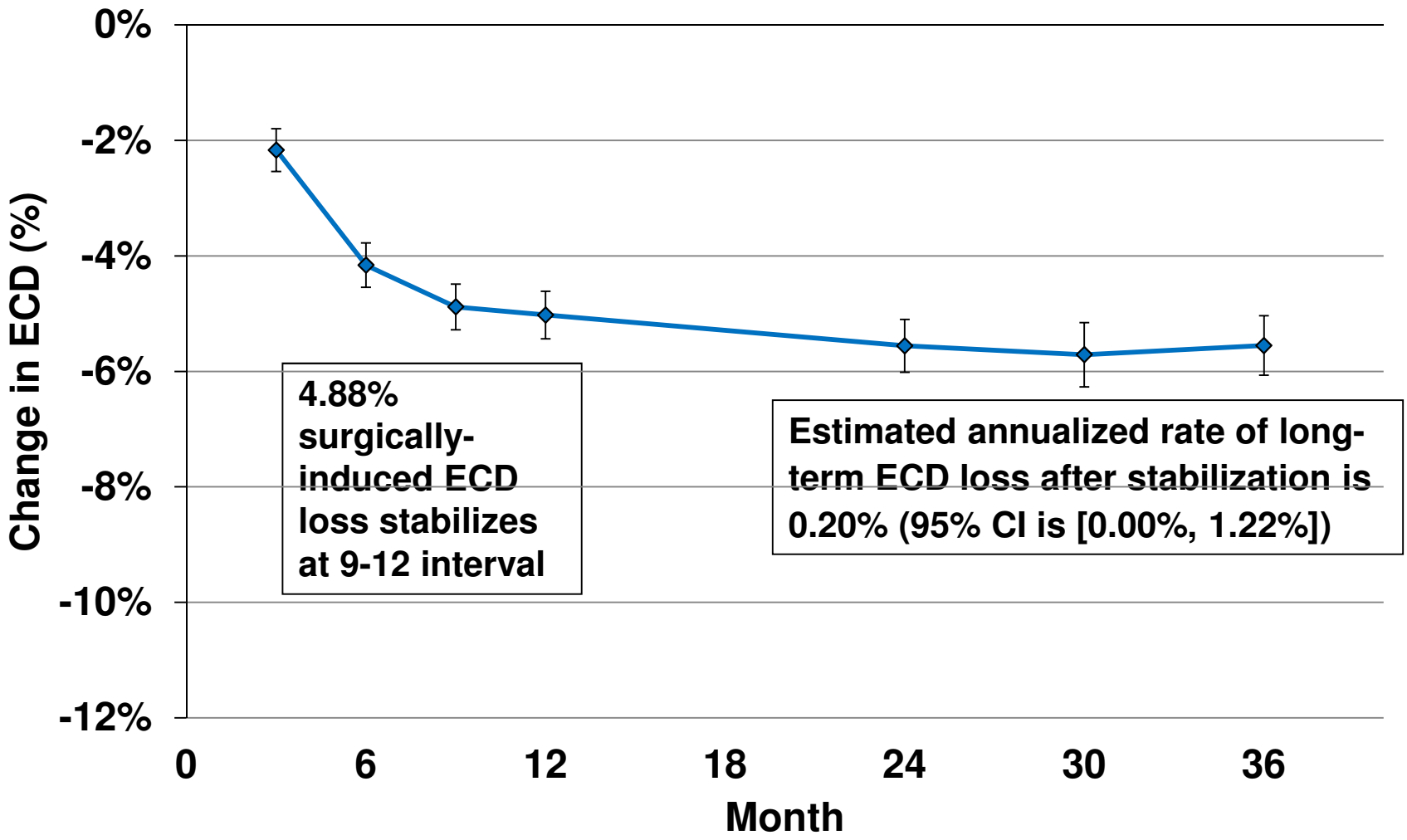
	Symptom	Large mesopic pupil size (≥6.0 mm) n = 193 Mean (SD)	Small mesopic pupil size (<6.0mm) n = 283 Mean (SD)
Ghosting	Pre-op	0.06 (0.49)	0.06 (0.38)
	12 months	0.60 (1.32)	0.56 (1.29)
	Change: Pre to 12	0.54 (1.32)	0.49 (1.30)
Diplopia	Pre-op	0.02 (0.21)	0.05 (0.41)
	12 months	0.38 (1.08)	0.25 (0.89)
	Change: Pre to 12	0.36 (1.10)	0.19 (0.90)
Halos	Pre-op	0.07 (0.35)	0.11 (0.49)
	12 months	1.25 (1.64)	1.15 (1.74)
	Change: Pre to 12	1.19 (1.63)	1.04 (1.80)

Comparison of Symptoms as a Function of Mesopic Pupil Size.

Safety

- Primary Safety Parameters
  - BCDVA loss, induced astigmatism, and slit lamp findings of stromal haze
  - Adverse Events (AEs)
- Intraocular Pressure
- Contrast Sensitivity
- Patient Reported Symptoms
- **Endothelial Cell Density**

% Change in ECD From Baseline (Mean, 95% CI)



Safety Summary

- Persistent BCDVA loss of 0.6% at 12 months
  - Majority of BCDVA loss transient in nature
- Low rate of steroid-related IOP increases
- Decrease in monocular CS function as expected (still within normal ranges)
- No change in binocular CS function from baseline
- Minimal increases in postoperative symptoms reported on PRO
- Early surgical ECD loss with minimal estimated long-term loss

Presentation Agenda

Introduction	**Nick Tarantino, OD** *Chief Clinical & Regulatory Officer* *AcuFocus, Inc.*
Clinical Landscape	**Vance Thompson, MD** *Clinical Investigator*
Study Design	**Corina van de Pol, OD, PhD** *VP Clinical Research* *AcuFocus, Inc.*
Effectiveness	**John A Vukich, MD** *Clinical Investigator*
Safety	**Jay Pepose, MD, PhD** *Clinical Investigator*
Optimization of Surgical Procedure	**Dan Durrie, MD** *Clinical Investigator*
Benefit/Risk Conclusions	**John A Vukich, MD** *Clinical Investigator*

Optimization of Surgical Procedure

Daniel S. Durrie, MD

Clinical Professor, Kansas University
Durrie Vision
Overland Park, Kansas

What have we learned during the clinical study?

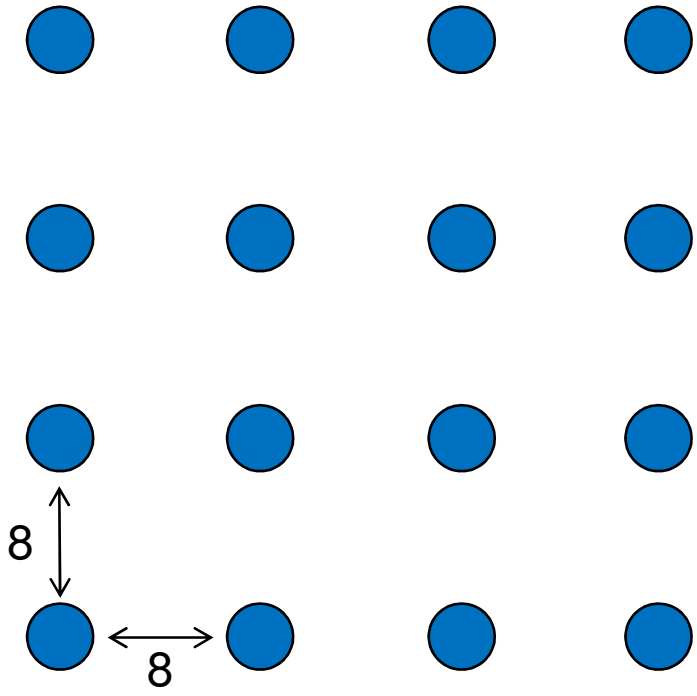
- Evolution of the surgical procedure
  - Optimizing the depth for inlay placement
    - Earlier clinical studies found rare corneal thinning with depth less than 170 microns
  - Corneal pockets vs. corneal flaps
  - Inlay removals
    - The inlay is removable
    - Patient's best corrected vision is preserved
    - Going forward, how can the surgeon decrease the incidence of refractive shift and the need for removal?
  - How to make the lamellar dissection

Wound Healing Response and Effects on Outcome

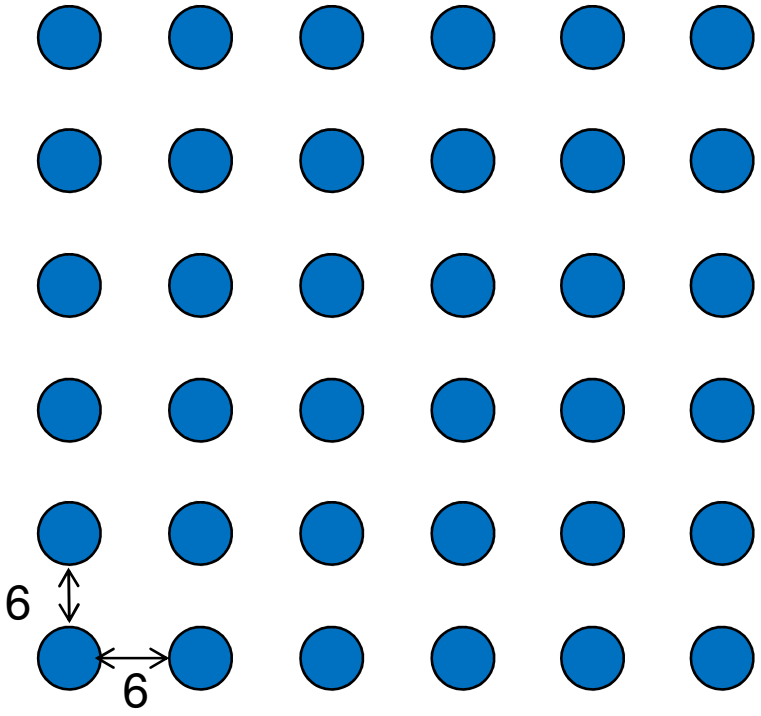
- Wound healing response is a normal postoperative reaction around any corneal inlay
- Why is it a concern?
  - Greater response usually leads to greater MRSE change (refractive shift) and corresponding decrease in UCNVA
- Modulating the degree of wound healing results in improvements for effectiveness and safety outcomes:
  - Refractive stability
  - UCNVA
  - BCDVA
  - Removals

Minimizing Wound Healing: Femtosecond Spot/Line Separation

- Cavitation bubbles from femtosecond laser treatment



8 microns × 8 microns

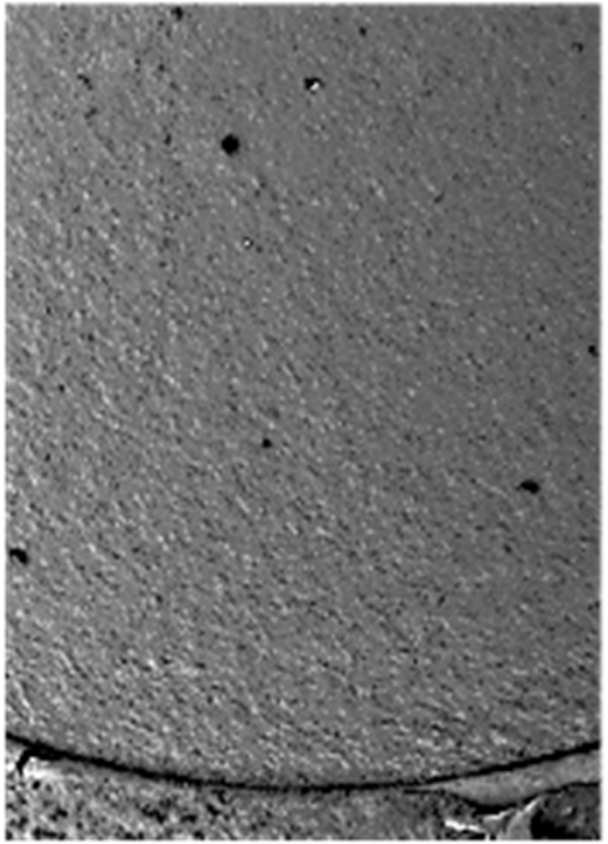


6 microns × 6 microns

- Closer spots = Smaller tissue bridges

Stromal Bed Quality Comparison Using SEM (30X)
Spot/Line Separation

8 µm × 8 µm



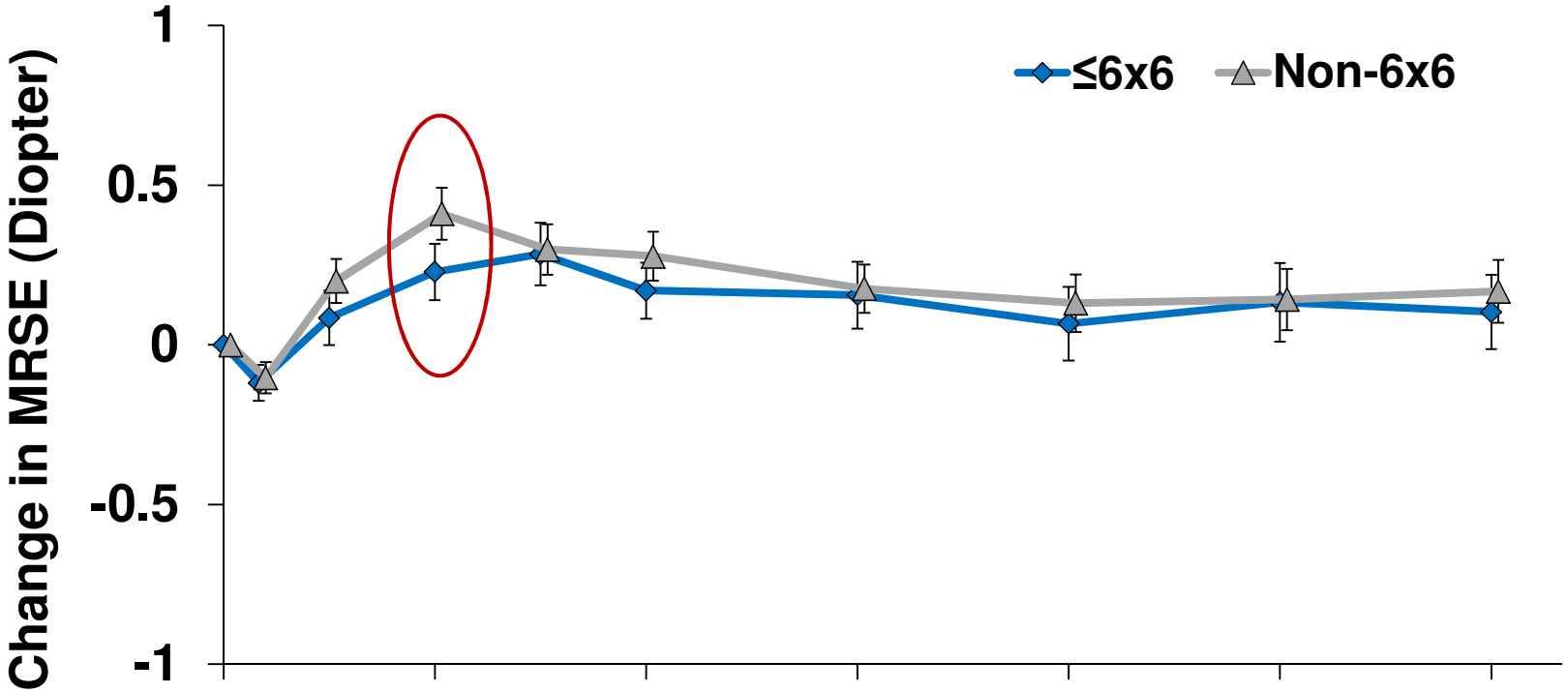
6 µm × 6 µm

All commercially available femtosecond lasers can perform 6×6 or tighter separation

Effectiveness Outcomes by Lamellar Resection Method

- Lamellar resection performed by each clinical site using each site's standard settings
  - Femtosecond laser
  - Mechanical microkeratome
  - No restrictions on model or manufacturer
- Effectiveness outcomes stratified by lamellar resection method
  - *Spot/line setting ≤6×6 (N = 175)*
  - *Spot/line setting non-6×6 (N = 332)*

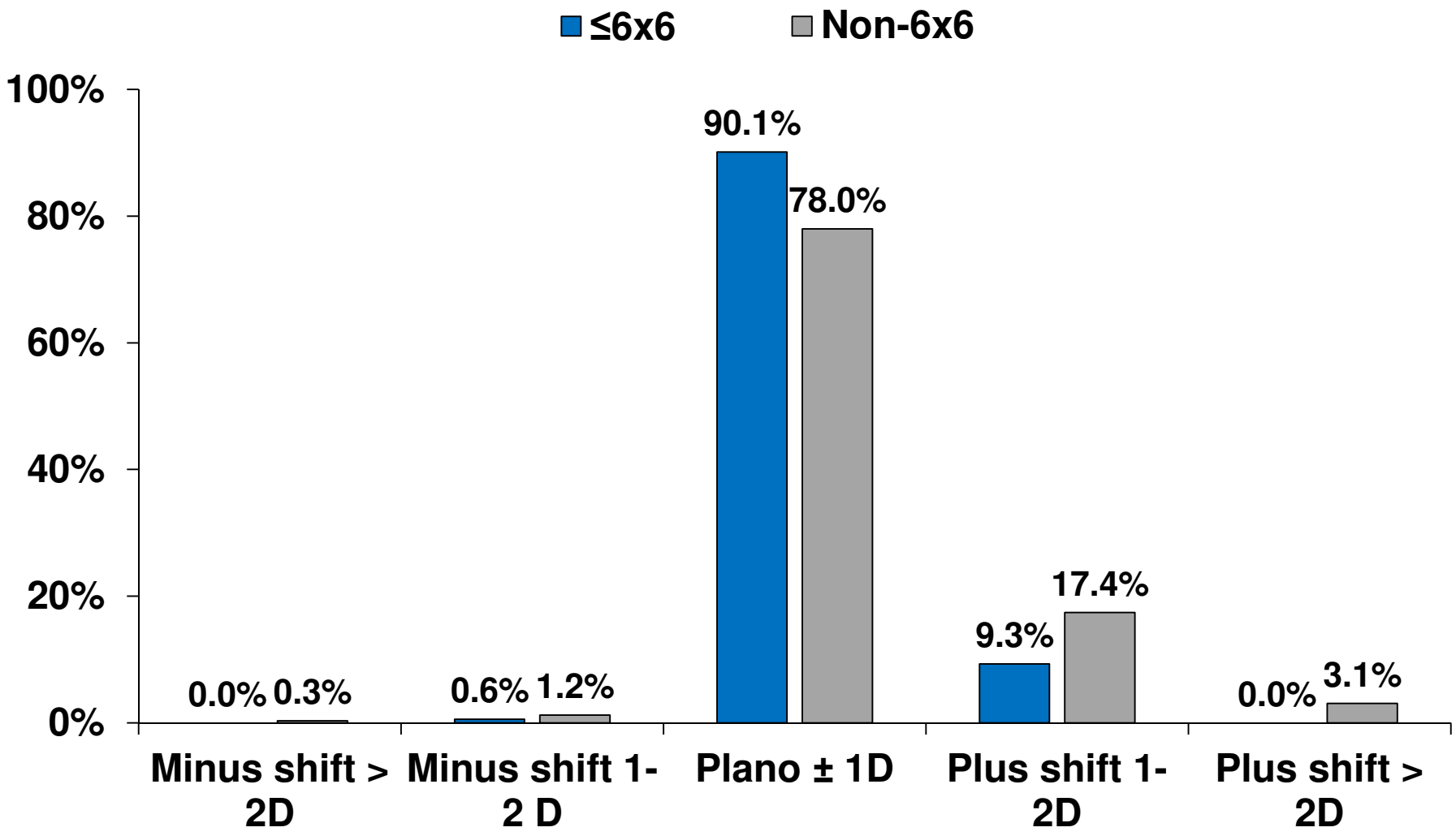
Change in MRSE: ≤6×6 and Non-6×6



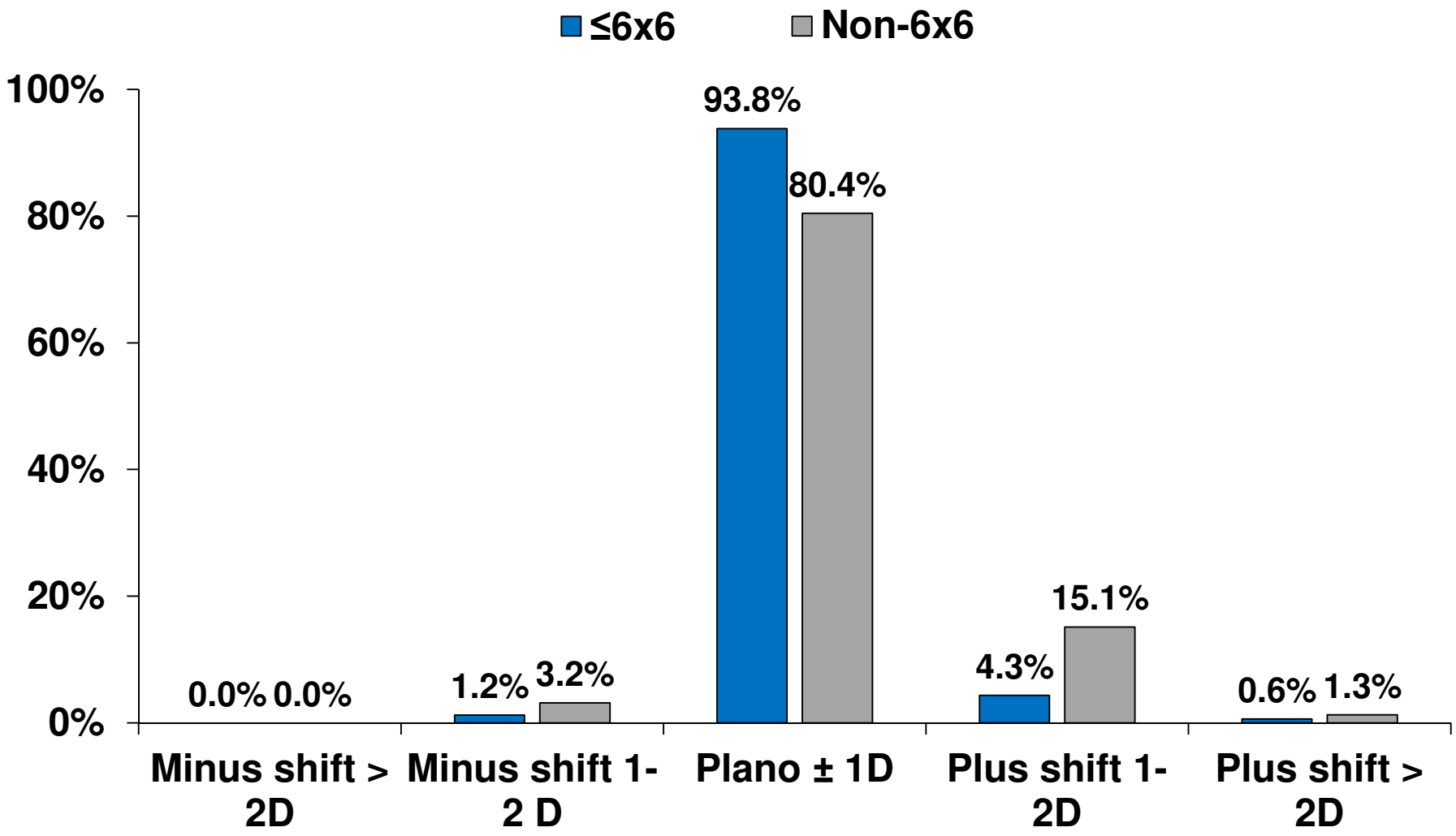
≤6×6	N = 175	172	162	160	158	152	153
Non-6×6	N = 333	327	317	289	284	252	271

Mean (95% CI)

Distribution of Change in MRSE from Baseline at 6 Months: ≤6x6 vs Non-6x6



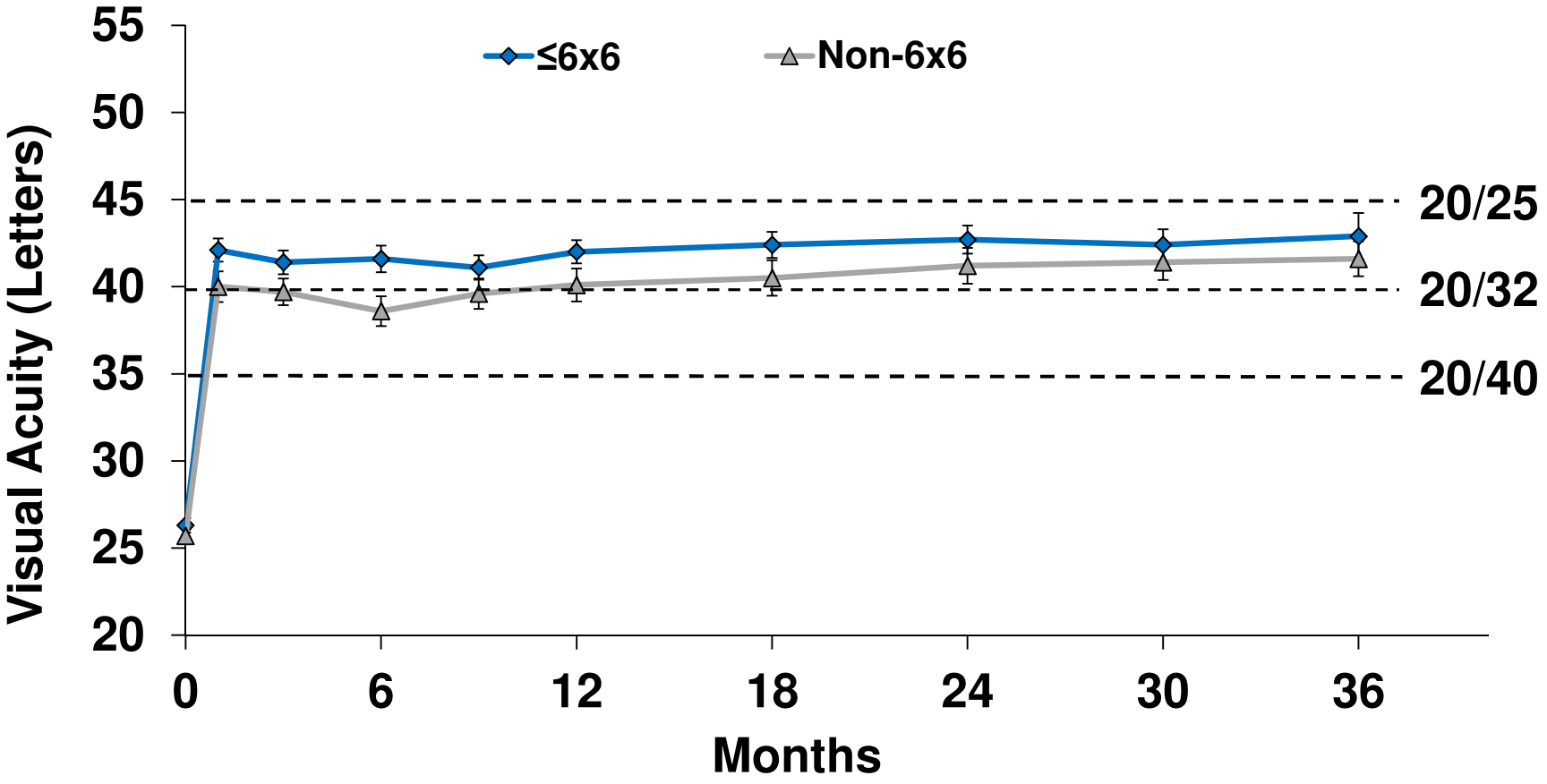
Distribution of Change in MRSE from Baseline at 12 Months: ≤6x6 vs Non-6x6



Refractive Stability: ≤6×6

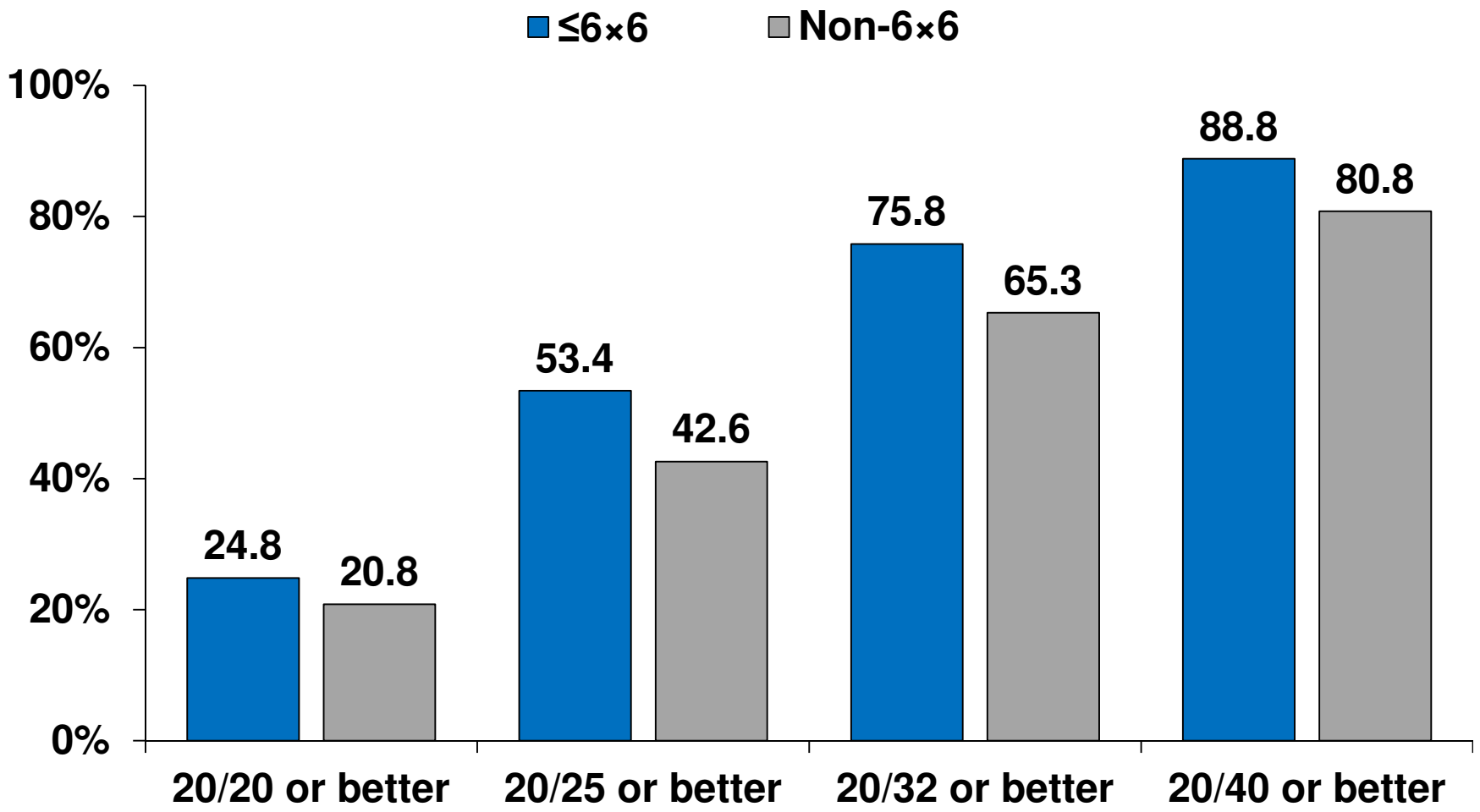
Criteria	Month-to-month interval when target was met:					
	6-9	9-12	12-18	18-24	24-30	30-36
≤1.00 D MRSE change between 2 consecutive visits				●	●	●
≤0.50 D per year (0.04 D/month) mean rate of change in MRSE	●	●	●	●	●	●
95% CI for the mean rate of change includes zero	●		●		●	●
Mean rate of change of MRSE over time, approaching zero (or a rate of change attributable to normal aging)					●	●

UCNVA: ≤6×6 and Non-6×6

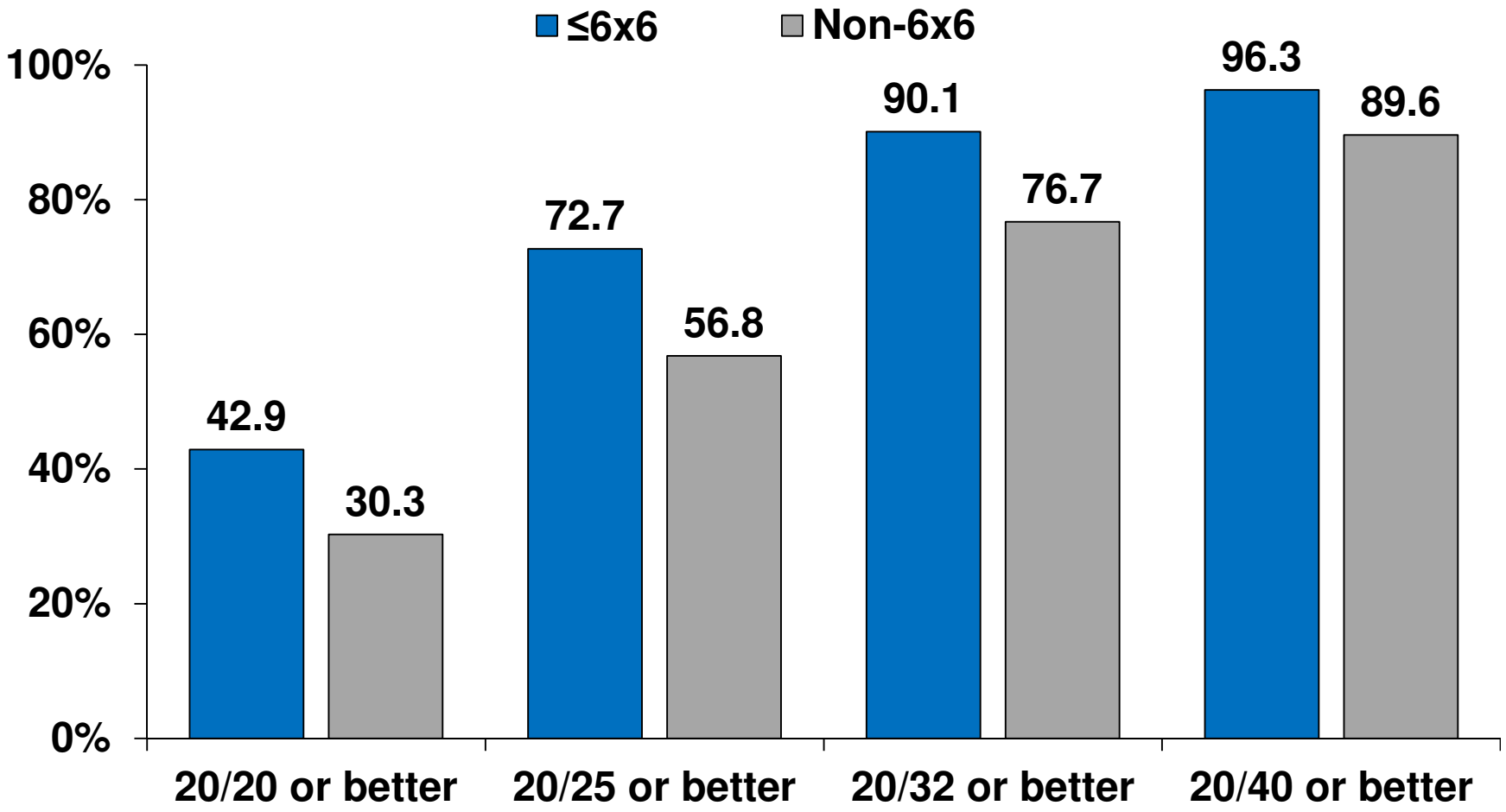


≤6×6	N = 175	172	161	158	157	151	152
Non-6×6	N = 333	327	317	286	279	247	265

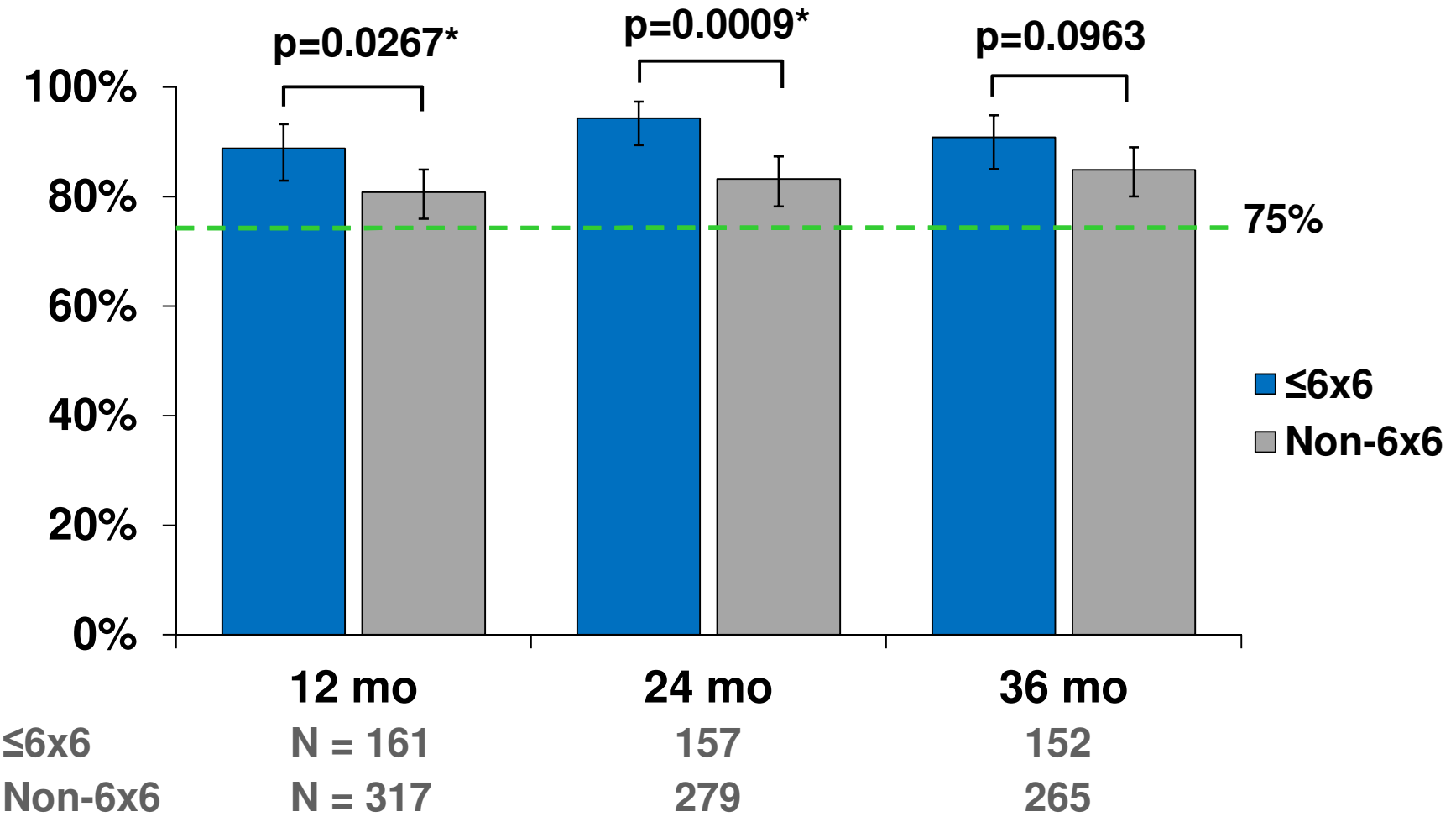
Distribution of Monocular UCNVA at 12 Months: ≤6×6 vs Non-6×6



Distribution of Binocular UCNVA at 12 Months: ≤6×6 vs Non-6×6



Monocular UCNVA of 20/40 or Better at Months 12, 24 and 36: ≤6×6 vs. Non-6×6



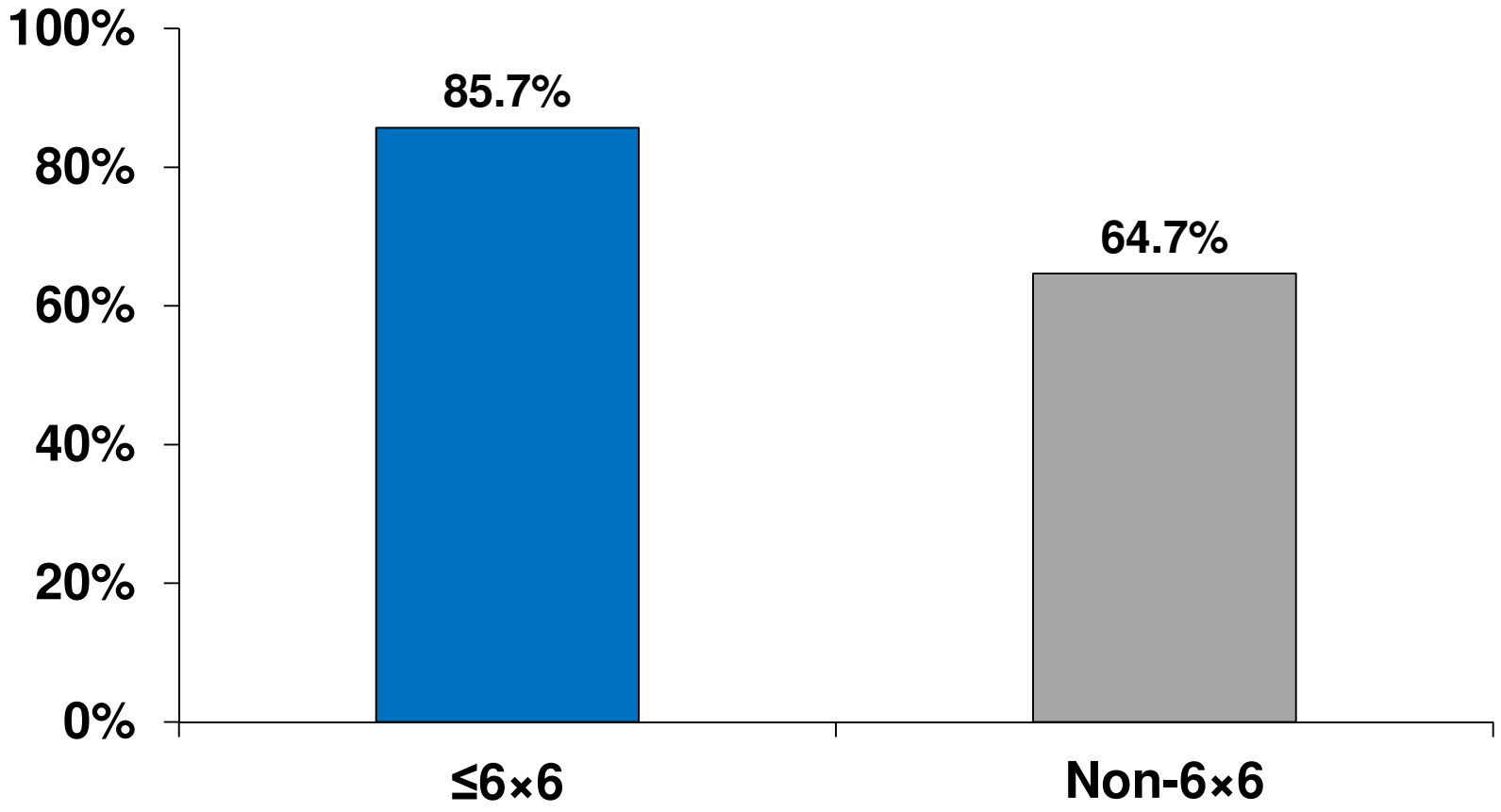
	12 mo	24 mo	36 mo
≤6x6	N = 161	157	152
Non-6x6	N = 317	279	265

*Statistically Significant - Fisher's Exact Test

P-values for 24 and 36 months not submitted to or reviewed by FDA

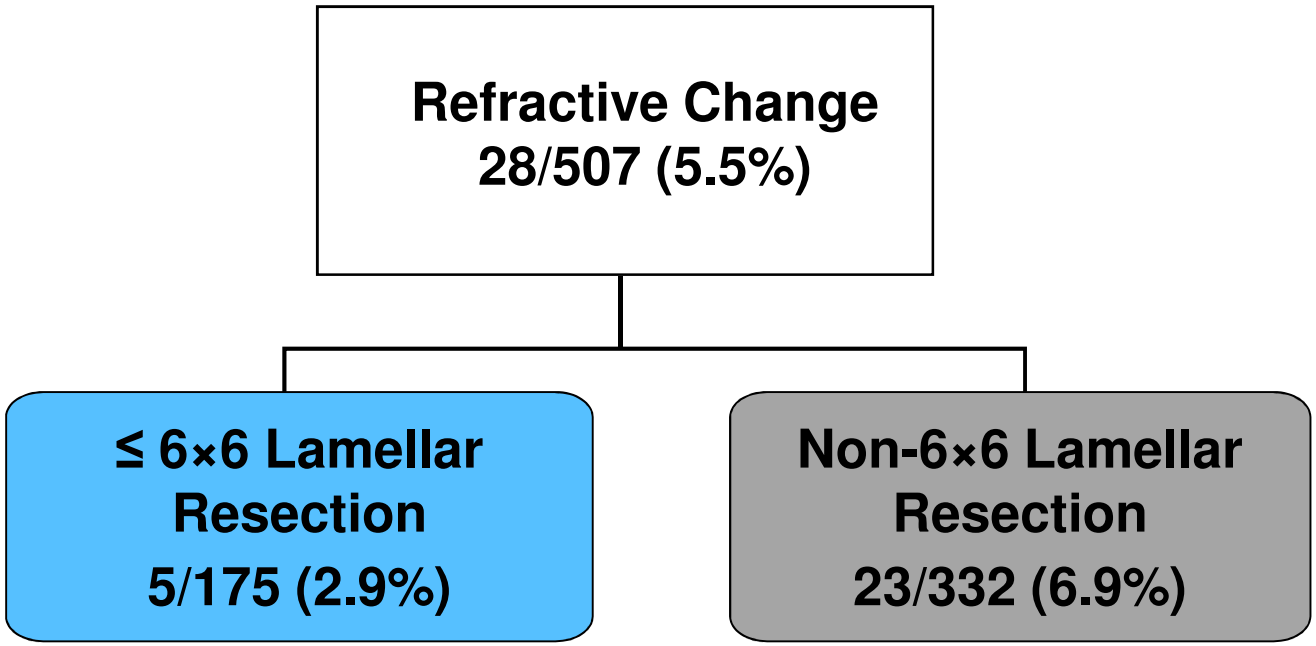
Post-hoc analysis

Satisfaction ≥4 with Near Vision Without Glasses Distribution at 12 Months: ≤6×6 vs Non-6×6



Impact of Surgical Technique on Removals

Removals: Refractive Change



- **Odds Ratio: Non-6×6 lamellar resection method is 2.53 (95% CI: 0.95, 6.78) times more likely to have removal than ≤6×6 method**

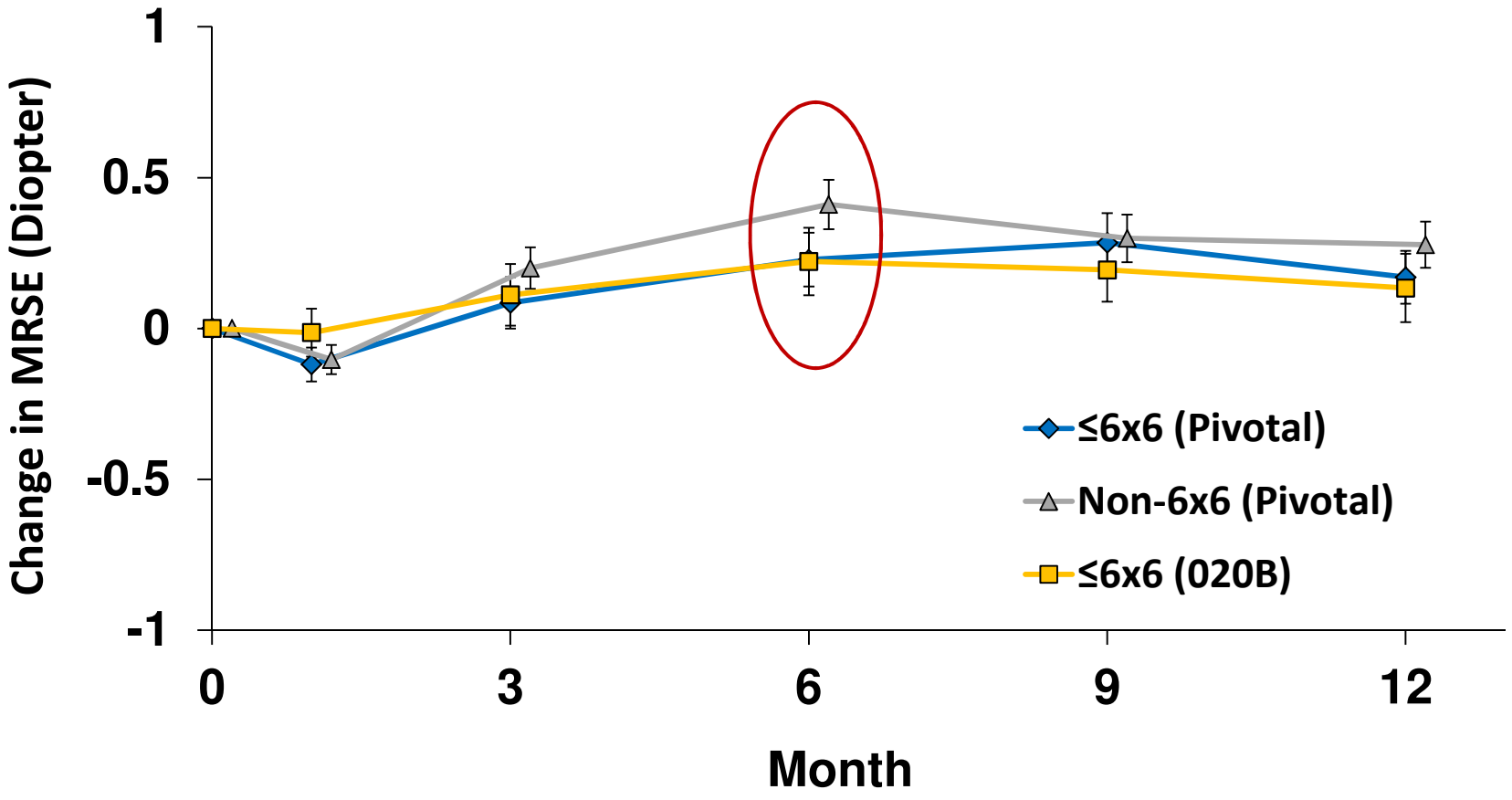
Odds ratio was not reviewed by FDA

Confirmatory Study – 020B

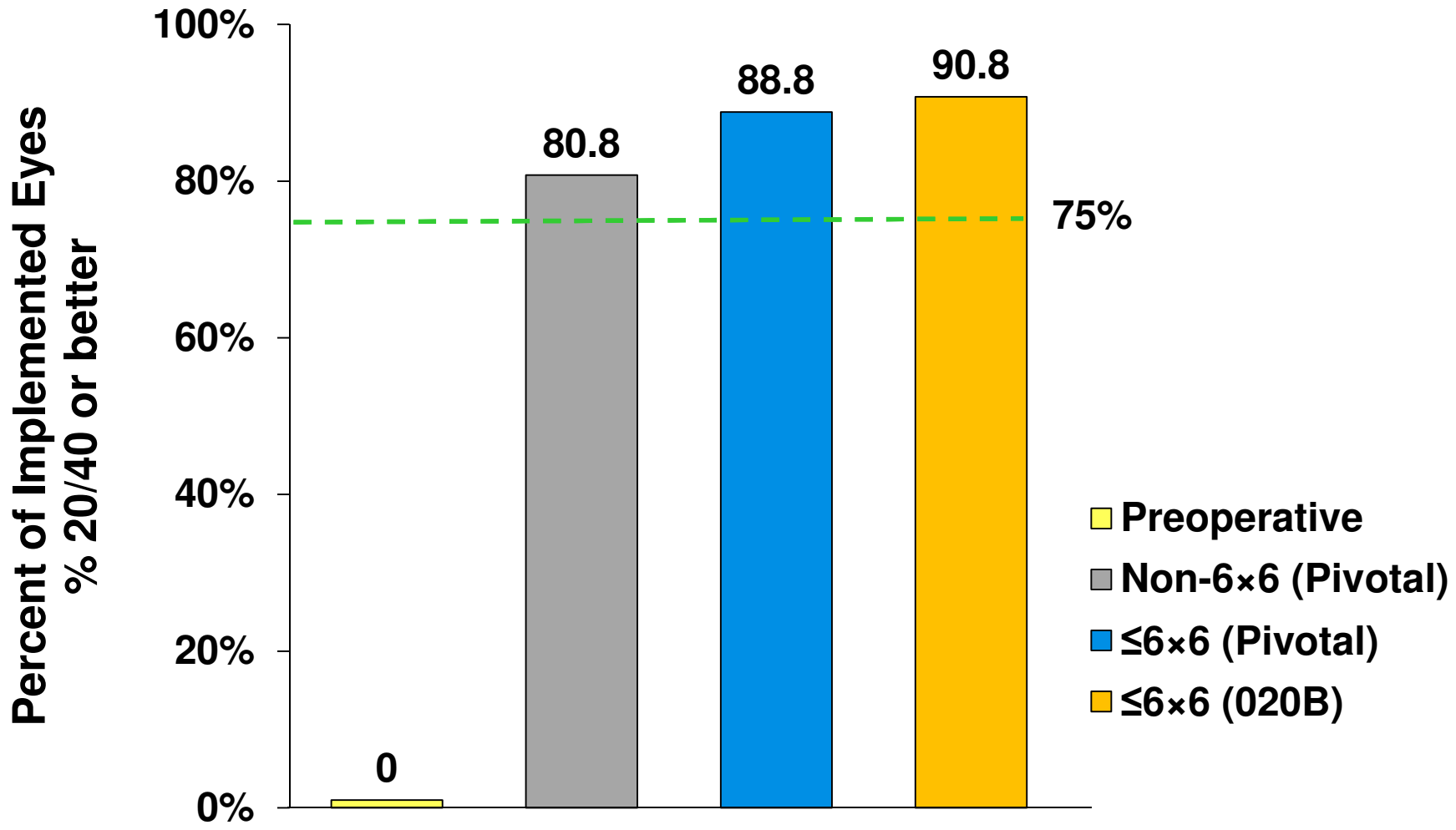
Confirmatory Study (020B): Key Points

- All lamellar resections in the confirmatory study were ≤6×6 spot/line separation
- 12 month study duration
- 151 subjects
- 12 OUS sites
- Same effectiveness endpoints as pivotal study

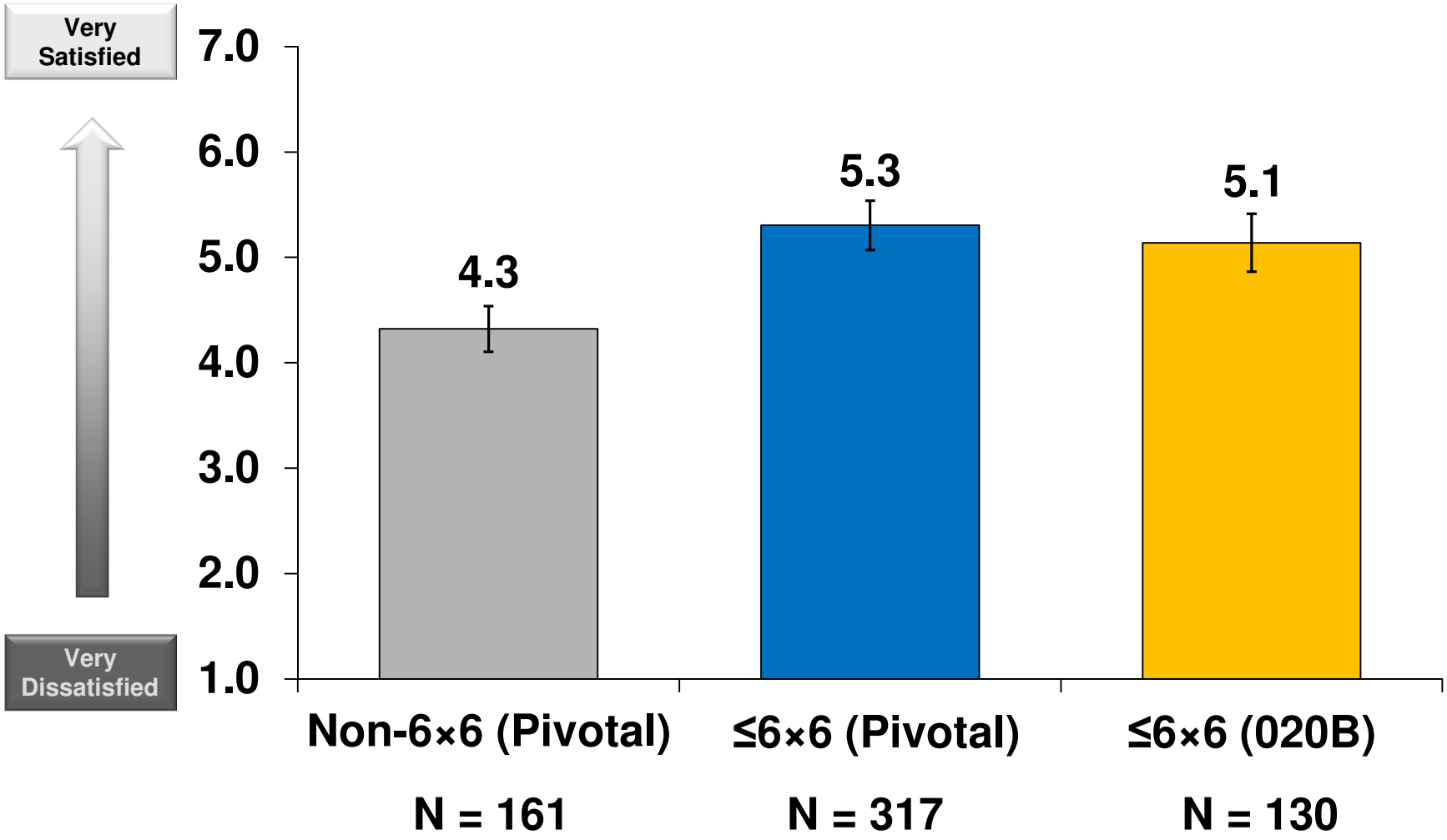
Change in MRSE through 12 Months



UCNVA (Implanted Eyes) at 12 Months



Satisfaction with Near Vision without Glasses



Comparison of Effectiveness Outcomes at 12 Months: Pivotal vs. Confirmatory Studies

	FDA Endpoint	IDE Non-6×6	IDE ≤6×6	020B ≤6×6
Primary Effectiveness Endpoint:				
*Effectiveness: % 20/40 or better UCNVA	≥75%	80.8% (256/317)	88.8% (143/161)	90.8% (118/130)
Secondary Effectiveness Endpoint:				
*Satisfaction without readers (rating of 4 or higher)	None	64.7% (205/317)	85.7% (138/161)	83.1% (108/130)

Comparison of Removals: Pivotal vs. Confirmatory Studies

	Pivotal Study Non-6×6 Group	Pivotal Study ≤6×6 Group	020B Study
Total Removals	10.5% (35/332)	5.1% (9/175)	6.0% (9/150)
Removals for Refractive Change	6.9% (23/332)	2.9% (5/175)	2.7% (4/150)

Summary Comparison Between ≤6×6 vs. Non-6×6

- Lower magnitude refractive shift at Month 6
- Better UCNVA outcomes at Months 12 and 24
- Better Satisfaction ratings
- Effectiveness findings from confirmatory study consistent with findings from ≤6×6 in the pivotal trial
- The ≤6×6 lamellar resection technique will be included in the labeling and surgical training

Presentation Agenda

Introduction	**Nick Tarantino, OD** *Chief Clinical & Regulatory Officer* *AcuFocus, Inc.*
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Optimization of Surgical Procedure	**Dan Durrie, MD** *Clinical Investigator*
Benefit/Risk Conclusions	**John A Vukich, MD** *Clinical Investigator*

Benefit/Risk

John A Vukich, MD

Clinical Investigator

Davis Duehr Dean

Madison, Wisconsin

Need for Safe and Effective Alternatives for the Treatment of Presbyopia

- With the increased visual demands of a growing presbyopic population, there is a need for a safe and effective surgical option that can reduce dependency on spectacles

Associations of Presbyopia With Vision-Targeted Health-Related Quality of Life

Peter J. McDonnell, MD; Paul Lee, MD, JD; Karen Spritzer; Anne S. Lindblad, PhD; Ron D. Hays, PhD
Arch Ophthalmol. 2003;121:1577-1581

- **"The 38 subjects in the 45 years of older age group scored significantly worse (P<.05) on 7 of the 13 subscales"**
  - **clarity of vision, expectations, near vision, diurnal fluctuations, symptoms, dependence on correction and satisfaction with correction**
- **"The NEI-RQL Instrument subscale scores indicate that presbyopia is associated with substantial, negative effects on vision-targeted health-related quality of life."**

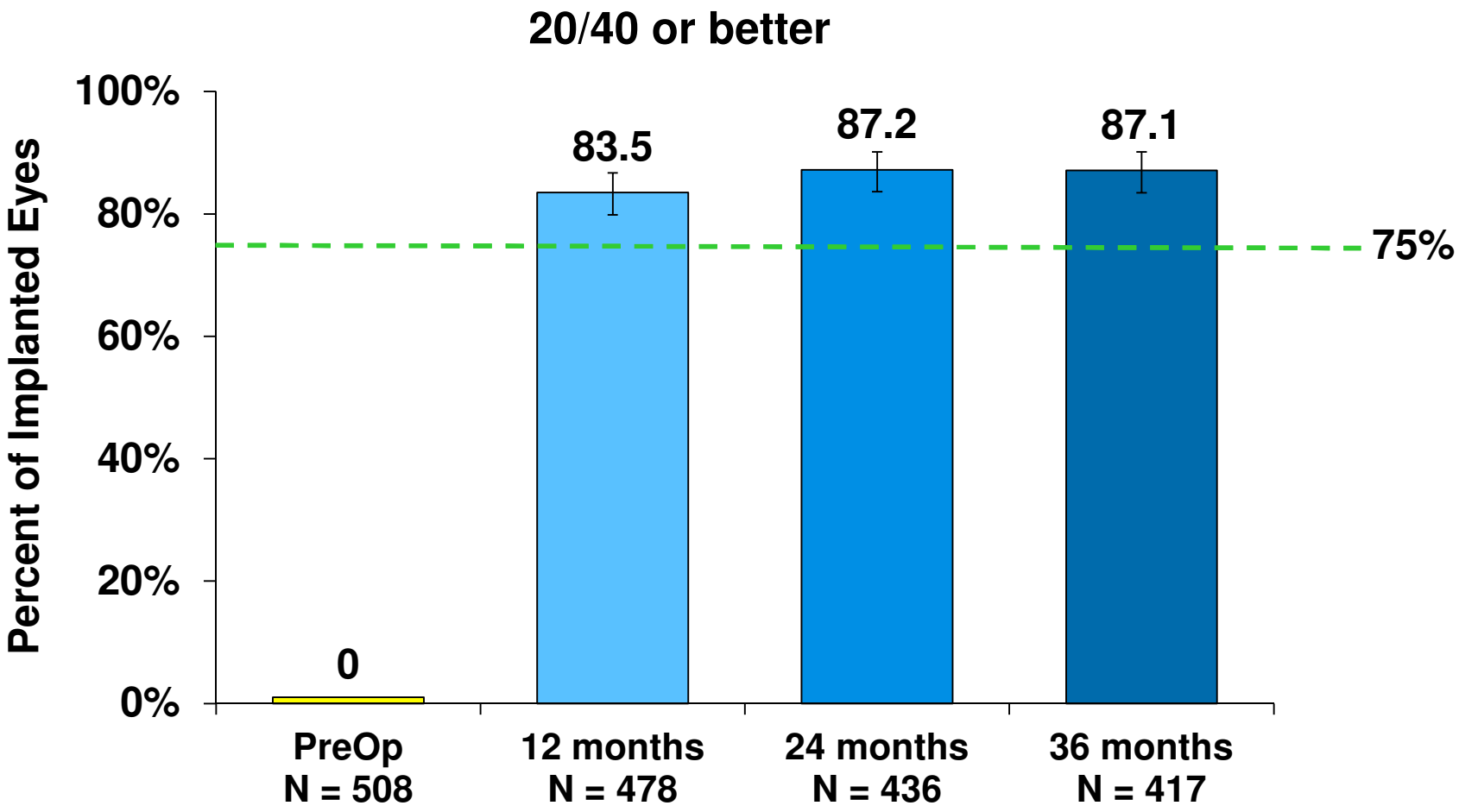
Primary Analysis for Primary Safety Outcomes at Month 12: Pivotal and Confirmatory Studies

Safety Parameters	Target	Pivotal Study Full Cohort	Pivotal Study ≤6×6 Group	020B Study
Persistent BCDVA loss of ≥ 2 lines at two consecutive visits	5%	0.6% (3/479)	0.0% (0/162)	0.7% (1/139)
BCDVA worse than 20/40 if 20/20 or better preoperatively	1%	0.0% (0/479)	0.0% (0/162)	0.0% (0/139)
Induced refractive astigmatism > 2.00 D	5%	0.0% (0/479)	0.0% (0/162)	0.0% (0/139)
Corneal haze in conjunction with BCDVA loss > 2 lines	1%	0.0% (0/479)	0.0% (0/162)	0.0% (0/139)

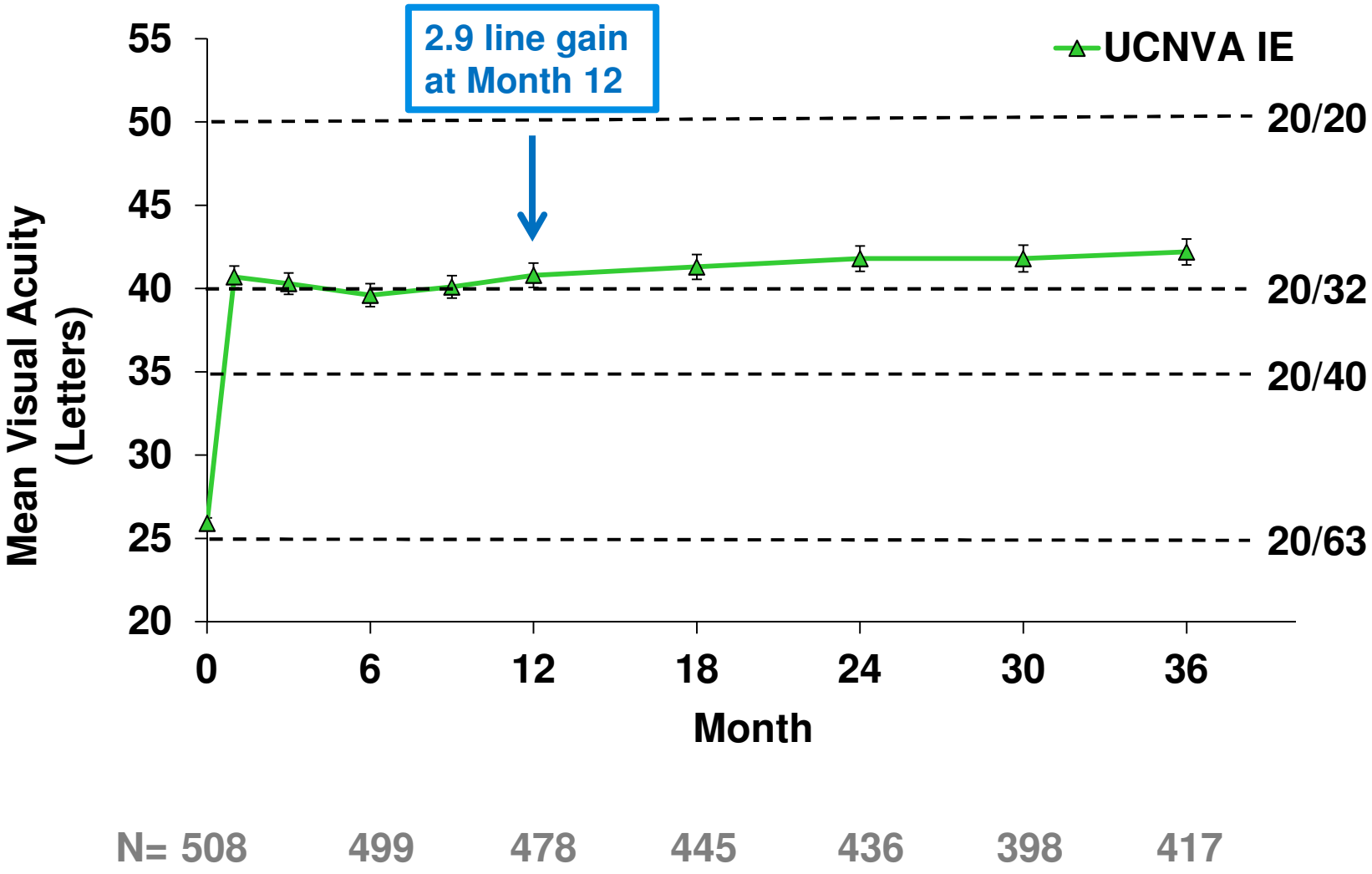
Safety Summary

- Low rate of steroid-related IOP increases
- Decrease in monocular CS function as expected
- No change in binocular CS function from baseline
- Minimal increases in postoperative symptoms reported on PRO
- Early surgical ECD loss with minimal estimated long-term loss

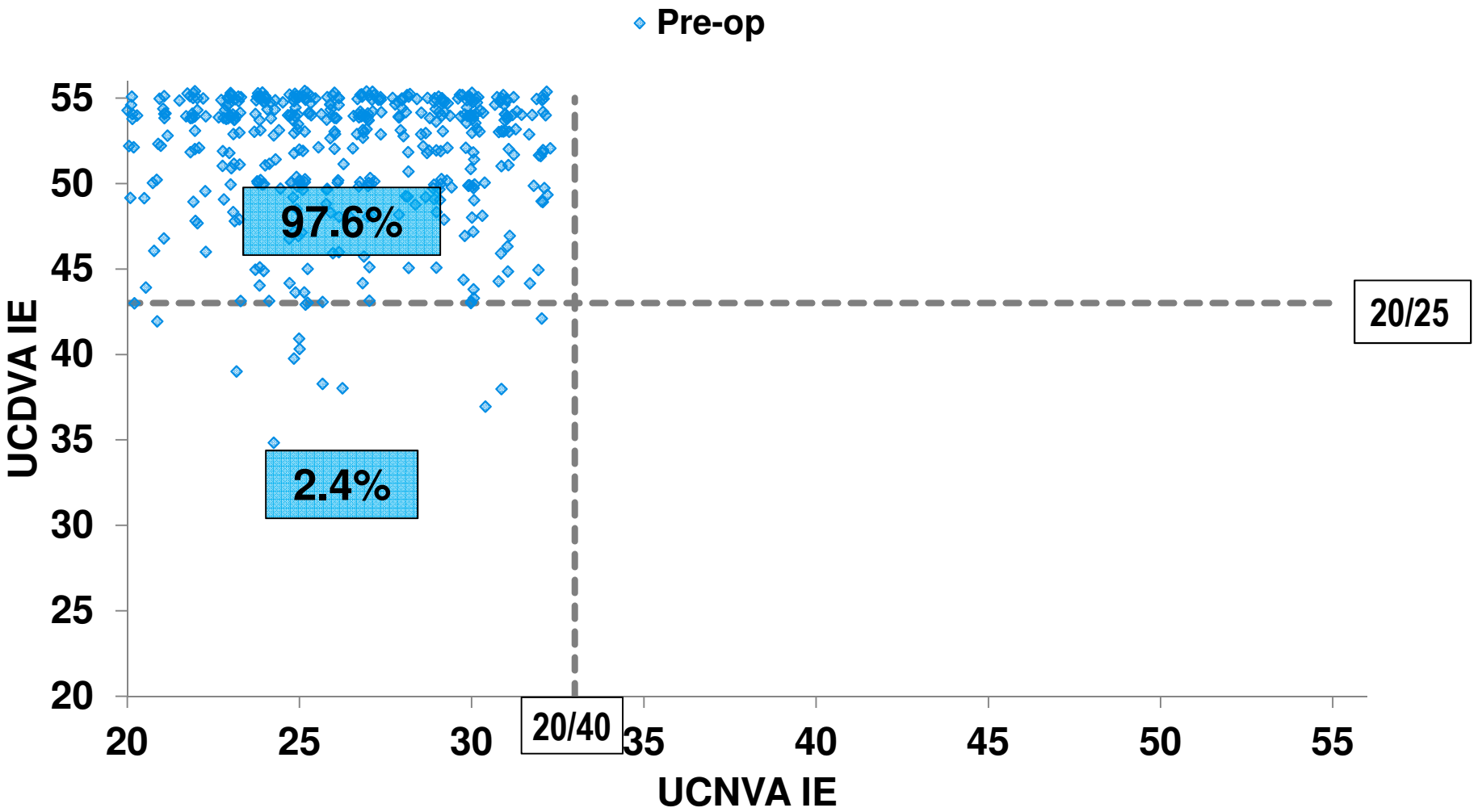
Primary Effectiveness Endpoint: Entire Cohort



Monocular UCNVA: Implanted Eyes

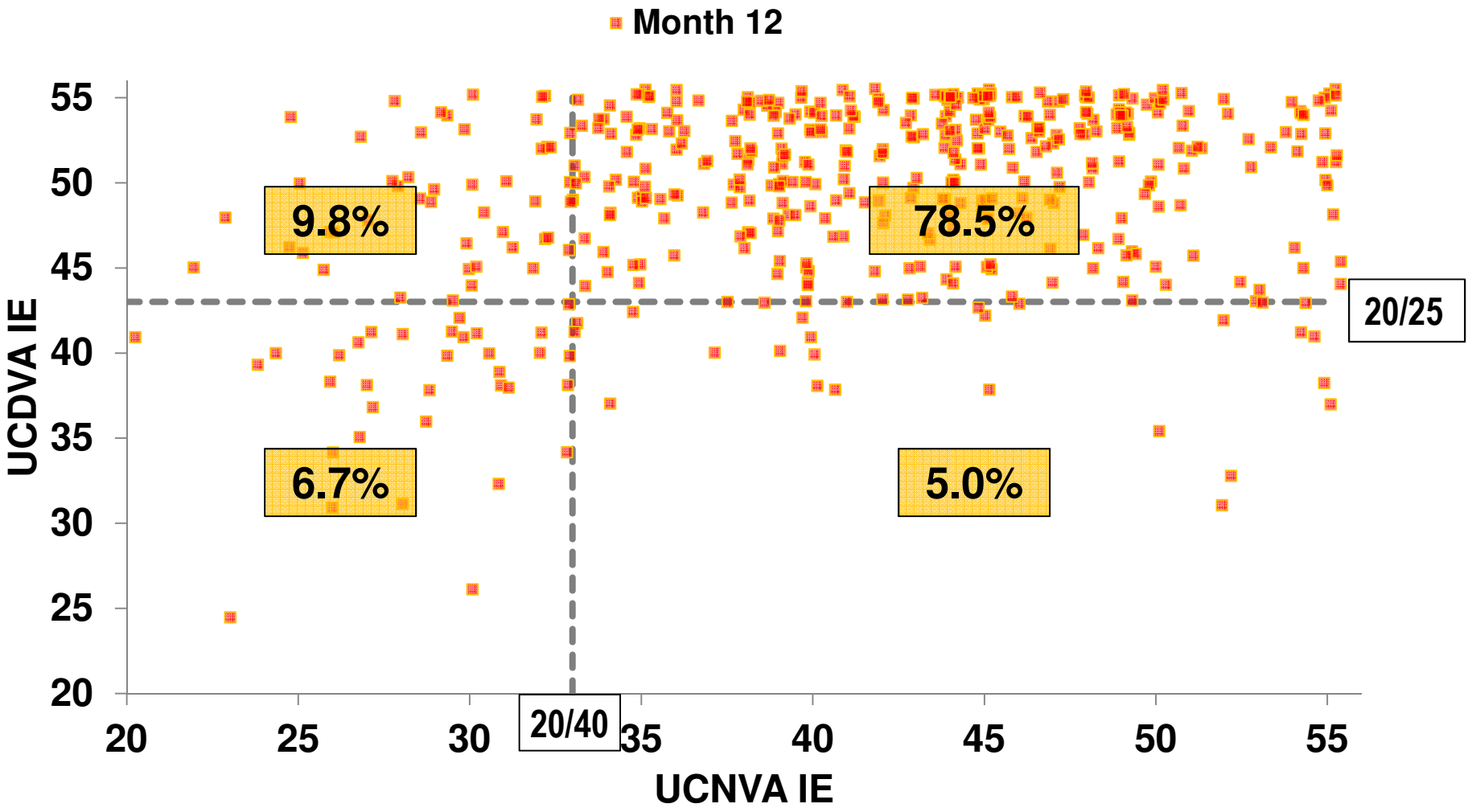


Pre-op Pivotal Study
Combined UCNVA and UCDVA



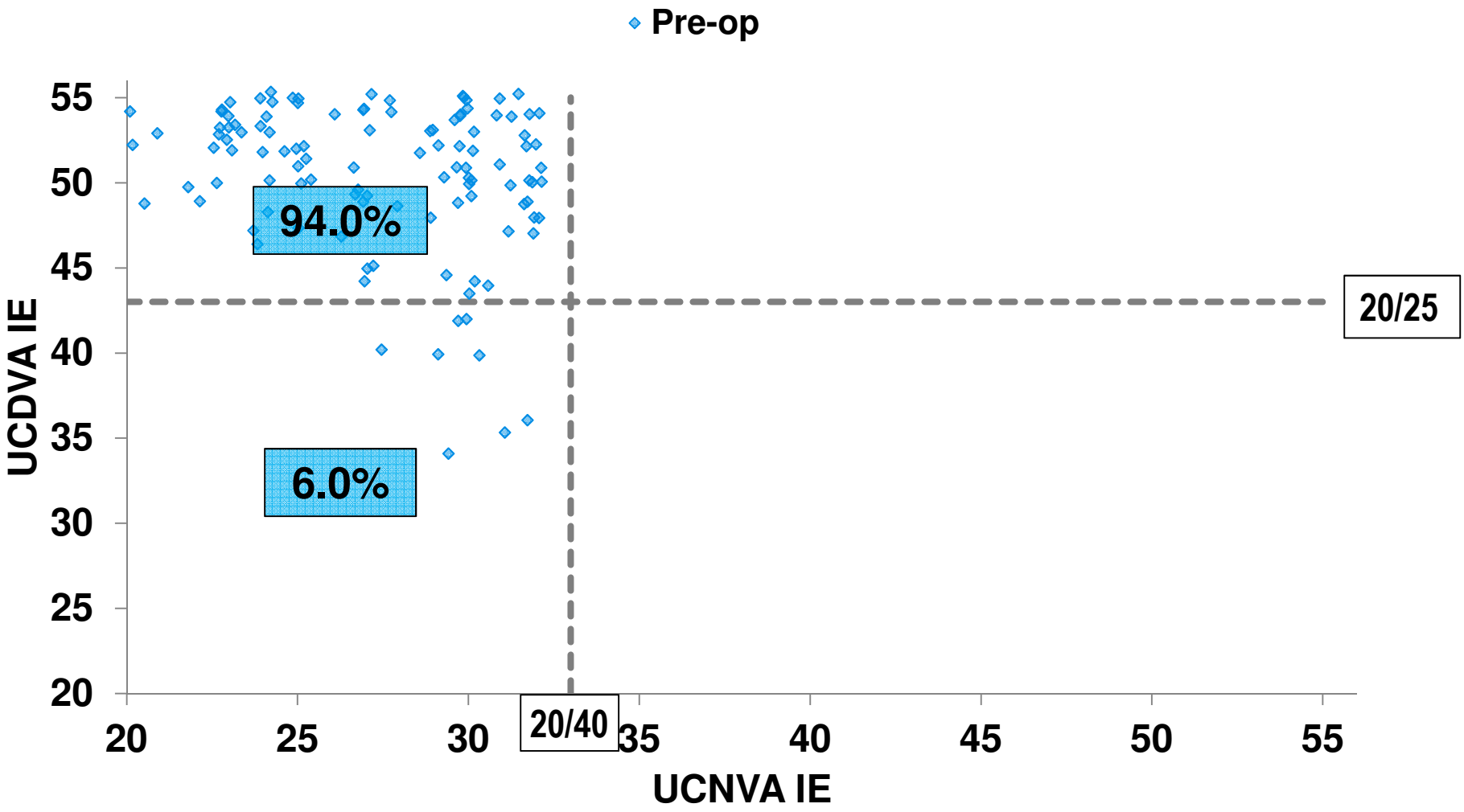
N = 478

Month 12 Post-op Pivotal Study Combined UCNVA and UCDVA



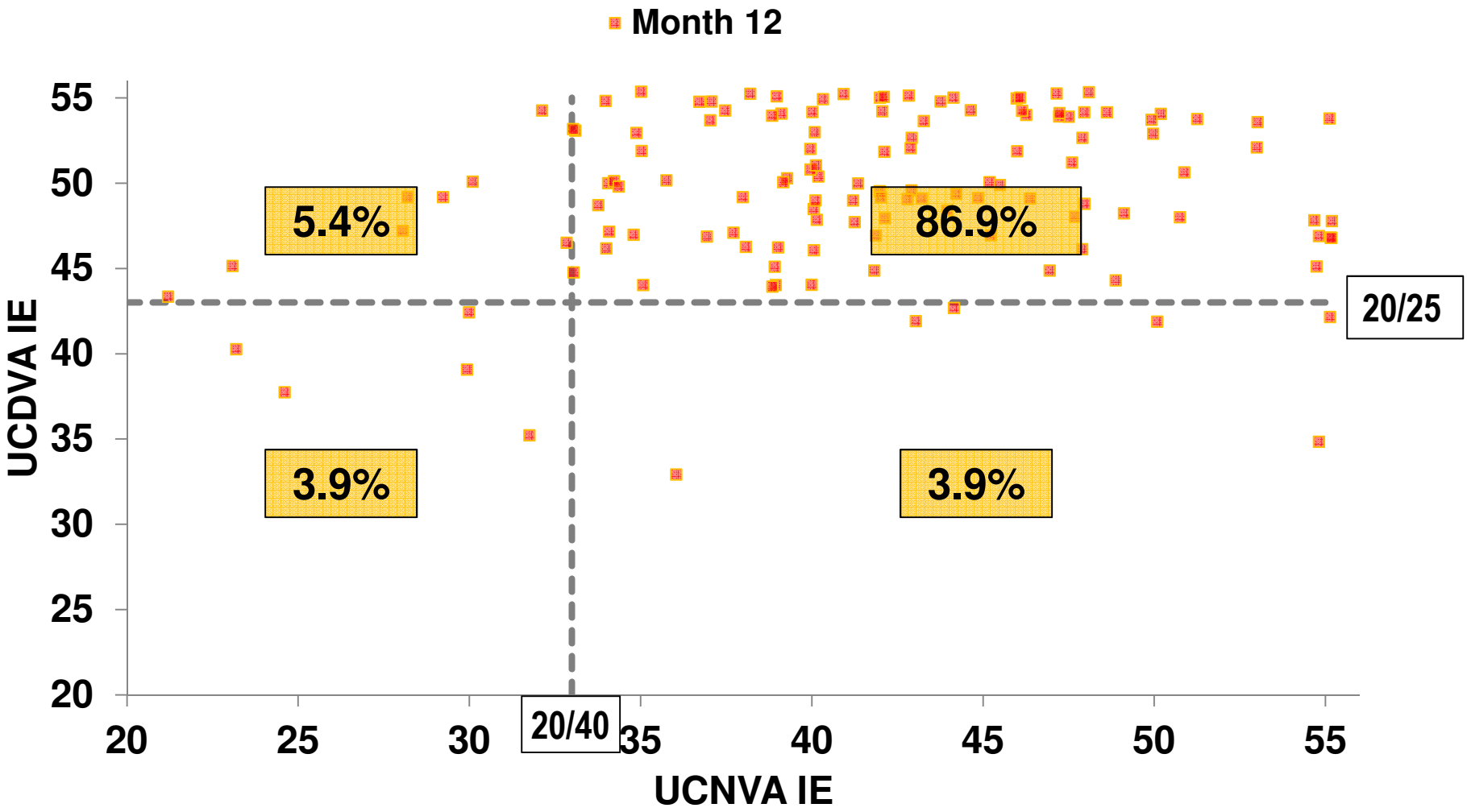
N = 478

Pre-op Confirmatory Study
Combined UCNVA and UCDVA (020B)



N = 130

Month 12 Post-op Confirmatory Study Combined UCNVA and UCDVA (020B)

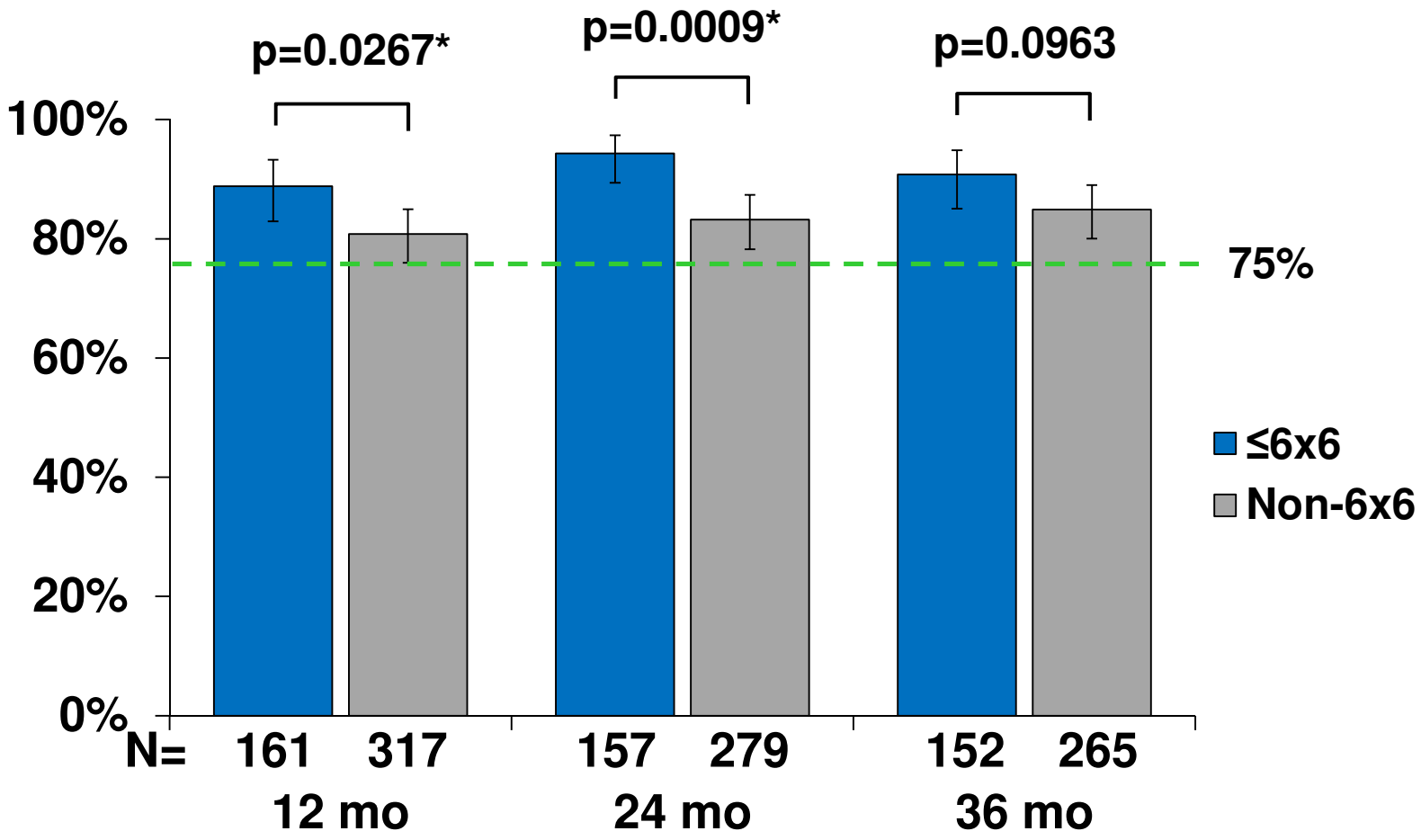


N = 130

Optimization of KAMRA Outcomes

- **Optimization of surgical technique and equipment**
  - **≤6×6 spot/line setting reduces removals and increases patient satisfaction**

Monocular UCNVA of 20/40 or Better at Months 12, 24 and 36: ≤6×6 vs. Non-6×6

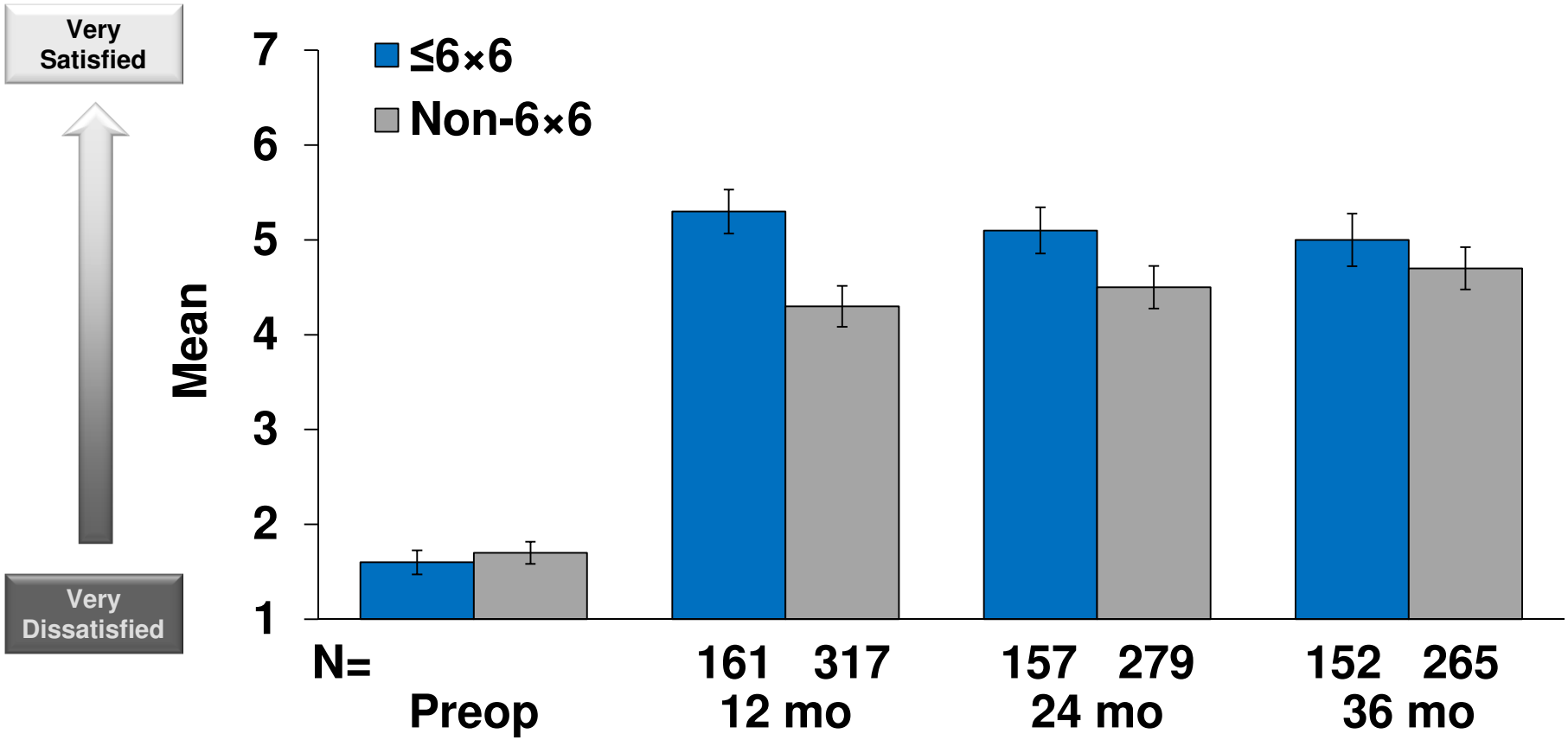


*Statistically Significant - Fisher's Exact Test

P-values for 24 and 36 months not submitted to or reviewed by FDA

Post-hoc analysis

Near Vision Satisfaction Without Near Rx: ≤6×6 vs. Non-6×6



Summary of Effectiveness Outcomes at Month 12: Pivotal and Confirmatory Studies

Effectiveness Parameters	Target	Pivotal Study Full Cohort	Pivotal Study ≤6×6 Group	020B Study
Primary Endpoint:				
*Effectiveness: % 20/40 or better UCNVA	≥75%	83.5% (399/478)	88.8% (143/161)	90.8% (118/130)
Secondary Endpoint:				
*Satisfaction without readers (rating of 4 or higher)	None	71.8% (343/478)	85.7% (138/161)	83.1% (108/130)

Benefit/Risk Summary

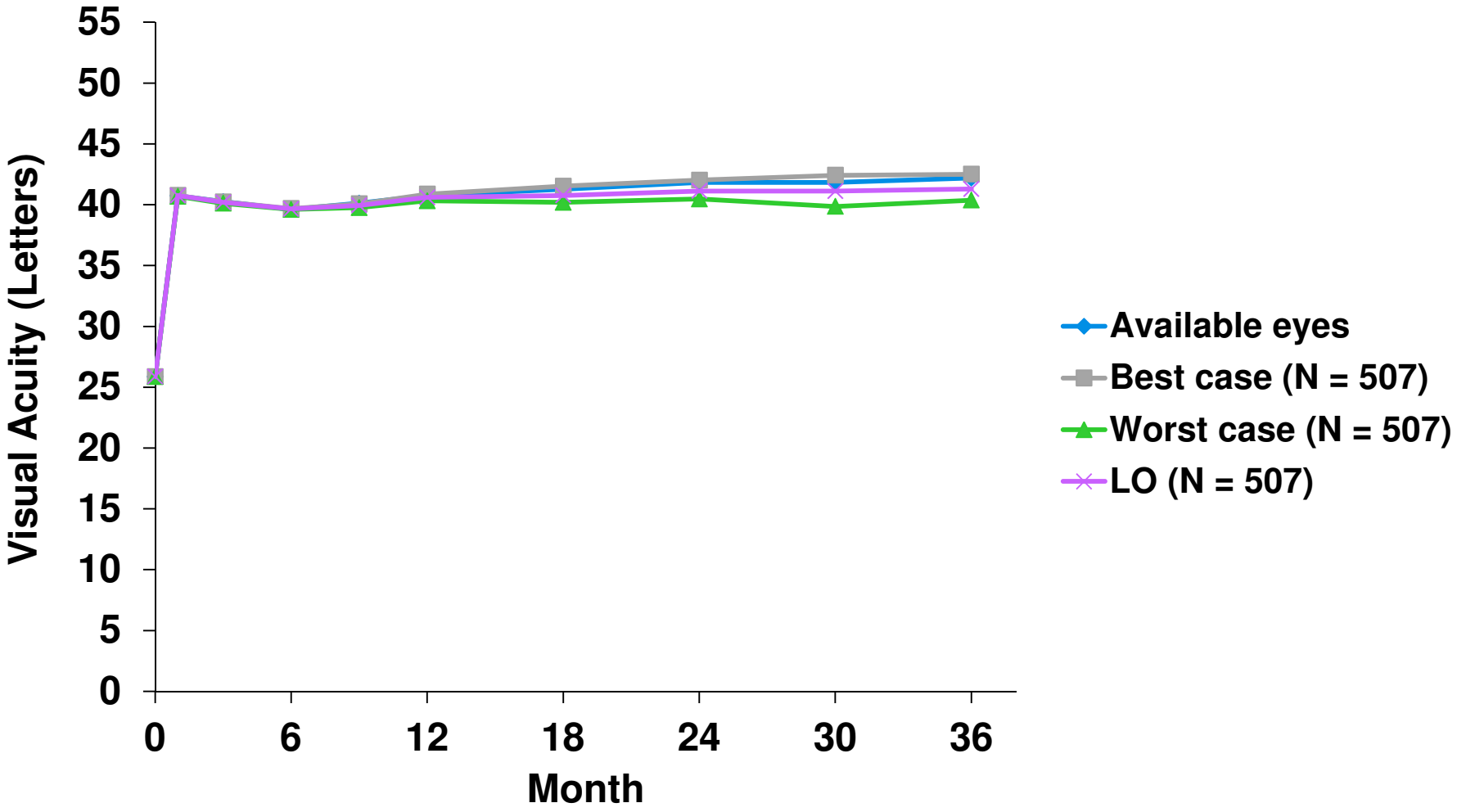
- Data for the total study population strongly support a favorable benefit/risk profile
- The ≤6×6 lamellar resection method had improved effectiveness and safety outcomes with fewer removals

KAMRA Inlay: Important Option for Treating Presbyopia

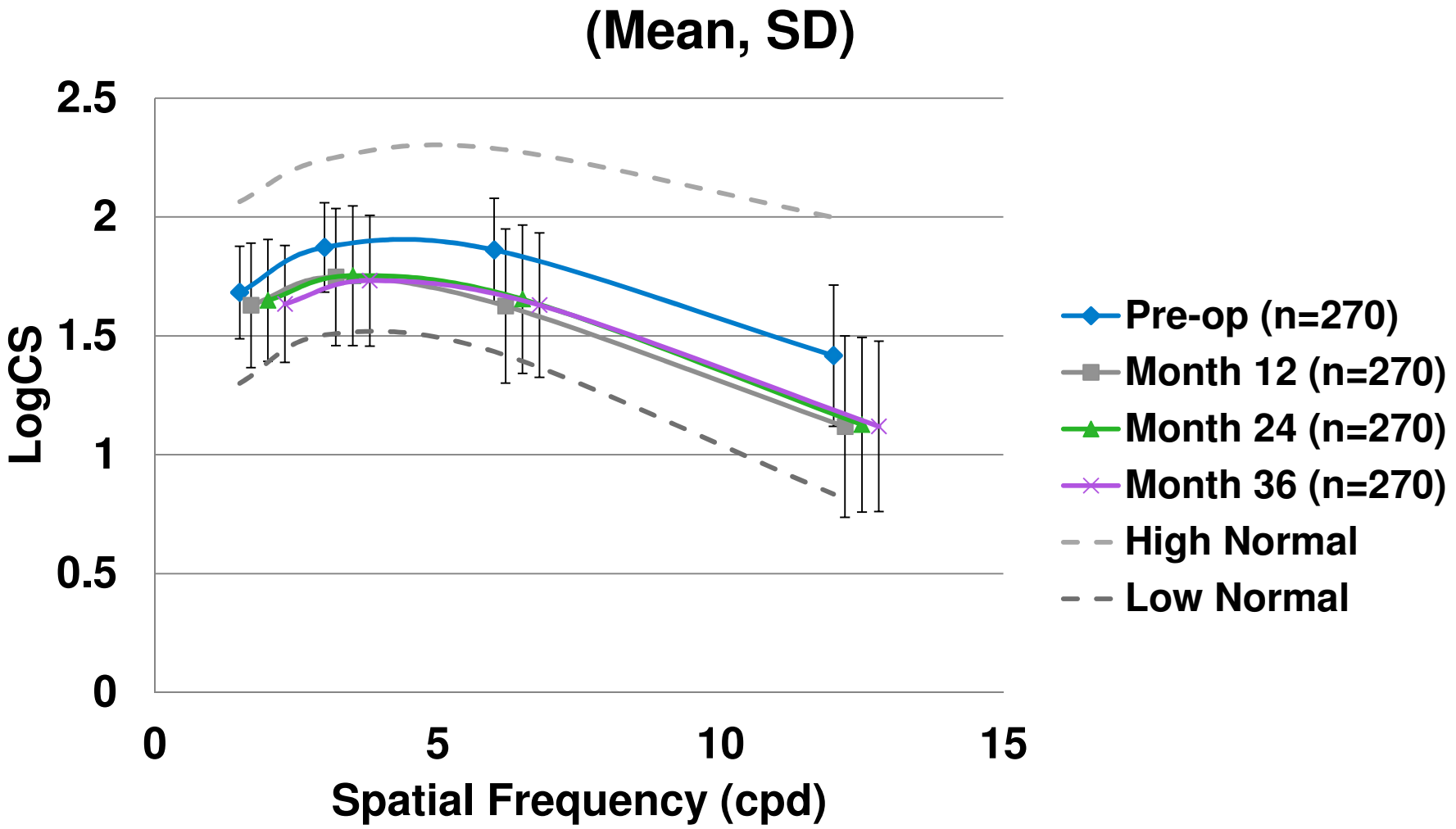
- The body of data provide reasonable assurance of safety and effectiveness of the KAMRA Inlay
- The KAMRA Inlay is an excellent new option for treating presbyopia, offering meaningful benefits with minimal risk to patients

Supporting Slides

UCNVA over Time
All Available Eyes and Imputed



Monocular Mesopic CS Without Glare (36 month consistent cohort)



Curves slightly offset for ease of comparison

Monocular Mesopic CS Without Glare Comparing Available eyes vs. 36 month consistent cohort

Cohort	Frequency	Preop	Month 3	Month 6	Month 12	Month 24	Month 36
Available eyes	**N**	**335**	**327**	**327**	**313**	**286**	**282**
36 mo CC	**N**	**270**	**270**	**270**	**270**	**270**	**270**
Available eyes	**1.5 cpd** Mean (SD)	1.679 (0.198)	1.610 (0.269)	1.602 (0.270)	1.612 (0.270)	1.636 (0.262)	1.628 (0.248)
36 mo CC	**1.5 cpd** Mean (SD)	1.682 (0.195)	1.632 (0.248)	1.620 (0.258)	1.628 (0.262)	1.649 (0.256)	1.634 (0.246)
Available eyes	**3.0 cpd** Mean (SD)	1.872 (0.195)	1.681 (0.296)	1.696 (0.320)	1.742 (0.285)	1.742 (0.301)	1.727 (0.281)
36 mo CC	**3.0 cpd** Mean (SD)	1.872 (0.188)	1.689 (0.298)	1.713 (0.318)	1.747 (0.288)	1.753 (0.294)	1.732 (0.275)
Available eyes	**6.0 cpd** Mean (SD)	1.856 (0.228)	1.570 (0.328)	1.598 (0.331)	1.625 (0.323)	1.653 (0.311)	1.622 (0.302)
36 mo CC	**6.0 cpd** Mean (SD)	1.861 (0.218)	1.586 (0.325)	1.608 (0.324)	1.625 (0.324)	1.654 (0.312)	1.629 (0.304)
Available eyes	**12.0 cpd** Mean (SD)	1.413 (0.298)	1.041 (0.376)	1.099 (0.377)	1.124 (0.378)	1.125 (0.359)	1.118 (0.354)
36 mo CC	**12.0 cpd** Mean (SD)	1.416 (0.297)	1.058 (0.383)	1.101 (0.382)	1.118 (0.377)	1.126 (0.367)	1.119 (0.358)

Five-year Refractive Changes in an Older Population: The Blue Mountains Eye Study*

- Longitudinal study of 5-year change in refraction in subjects 49 years of age and older (3654 residents)
- Findings:
  - 49-54 years old: +0.41 D shift

**Magdalena Guzowski, BSc (Med), MBBS, Jie Jin Wang, MMed, PhD, Elena Rochtchina, MApplStat,Kathryn A. Rose, PhD, Paul Mitchell, MD, PhD. J Cataract Refract Surg. 2011;37:17291731.*

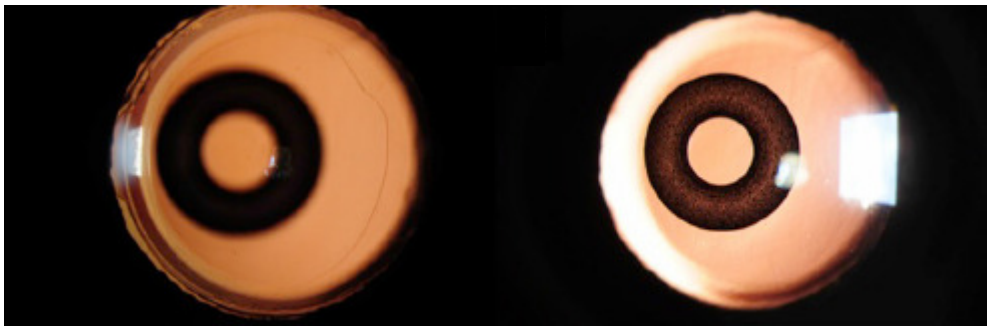
Open Access Full Text Article

CASE SERIES

Cataract surgery following KAMRA presbyopic implant

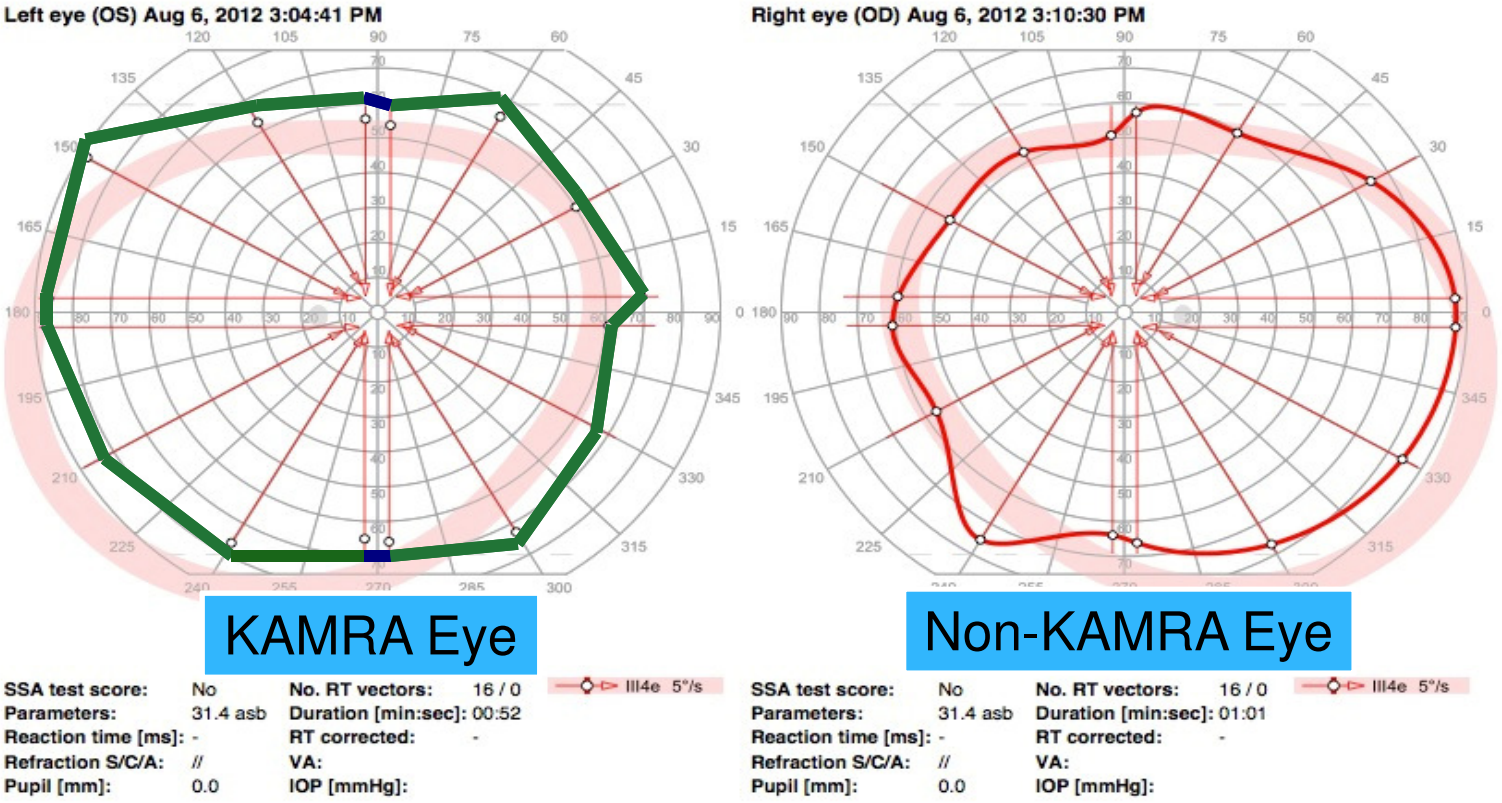
Tien-En Tan[1,2]
Jodhbir S Mehta[2–4]

Clinical Ophthalmology 2013:7 1899–1903



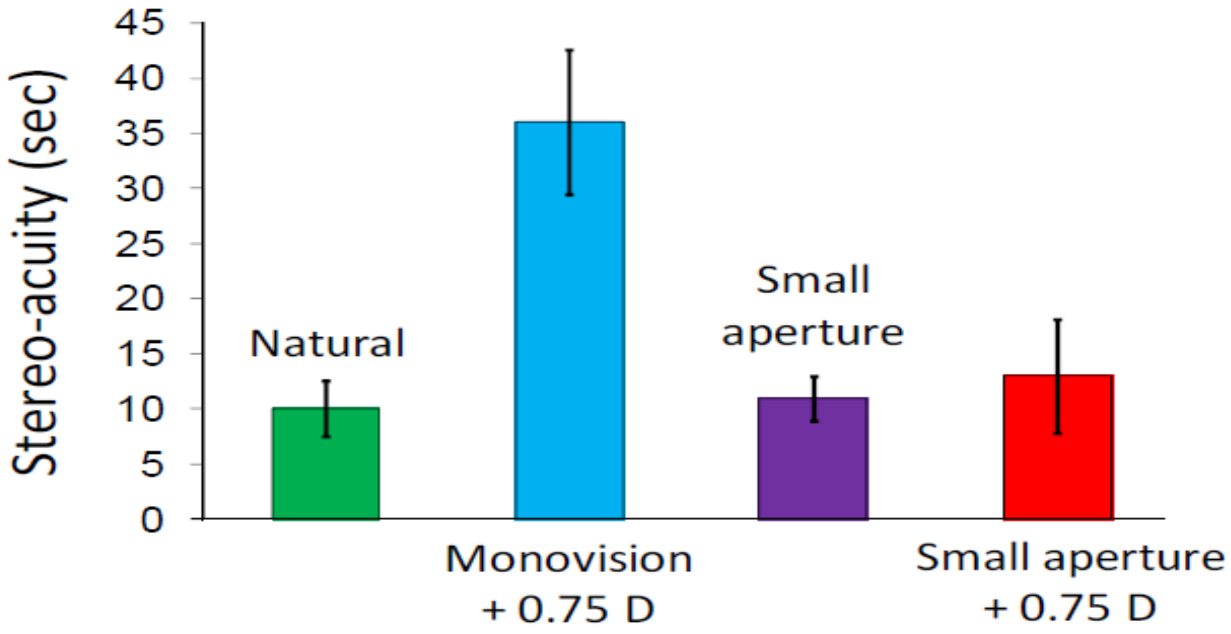
- **A case series of two KAMRA patients who developed visually significant cataracts**
- **No significant modifications to the surgical technique were required; surgeon reported no difference in ease of surgery or surgical time**
- **Biometry readings and SRK/T calculations were accurate**
- **Cataract surgery with the KAMRA implant left in situ is a viable option for patients**

Case Study


Left eye (OS) Aug 6, 2012 3:04:41 PM
KAMRA Eye
SSA test score: No
Parameters: 31.4 asb
Reaction time [ms]: -
Refraction S/C/A: //
Pupil [mm]: 0.0
No. RT vectors: 16 / 0
Duration [min:sec]: 00:52
RT corrected: -
VA:
IOP [mmHg]:
III4e 5°/s
Right eye (OD) Aug 6, 2012 3:10:30 PM
Non-KAMRA Eye
SSA test score: No
Parameters: 31.4 asb
Reaction time [ms]: -
Refraction S/C/A: //
Pupil [mm]: 0.0
No. RT vectors: 16 / 0
Duration [min:sec]: 01:01
RT corrected: -
VA:
IOP [mmHg]:
III4e 5°/s
OCTOPUS®
EyeSuite™ Kinetic, V2.3.0
OCTOPUS 900, SN 1,932, V 2.2.0 / 2.3.0
HAAG-STREIT INTERNATIONAL

Impact on Stereo Acuity: Monovision (MV) vs. Small Aperture (KAMRA Inlay) – Fernandez et al. (2013)

- Test conditions: Natural Vision (4 mm pupil), 0.75D MV, KAMRA Inlay, and KAMRA Inlay + 0.75D MV
- No impact on stereopsis from KAMRA Inlay
- KAMRA Inlay reduced negative impact of MV on stereopsis

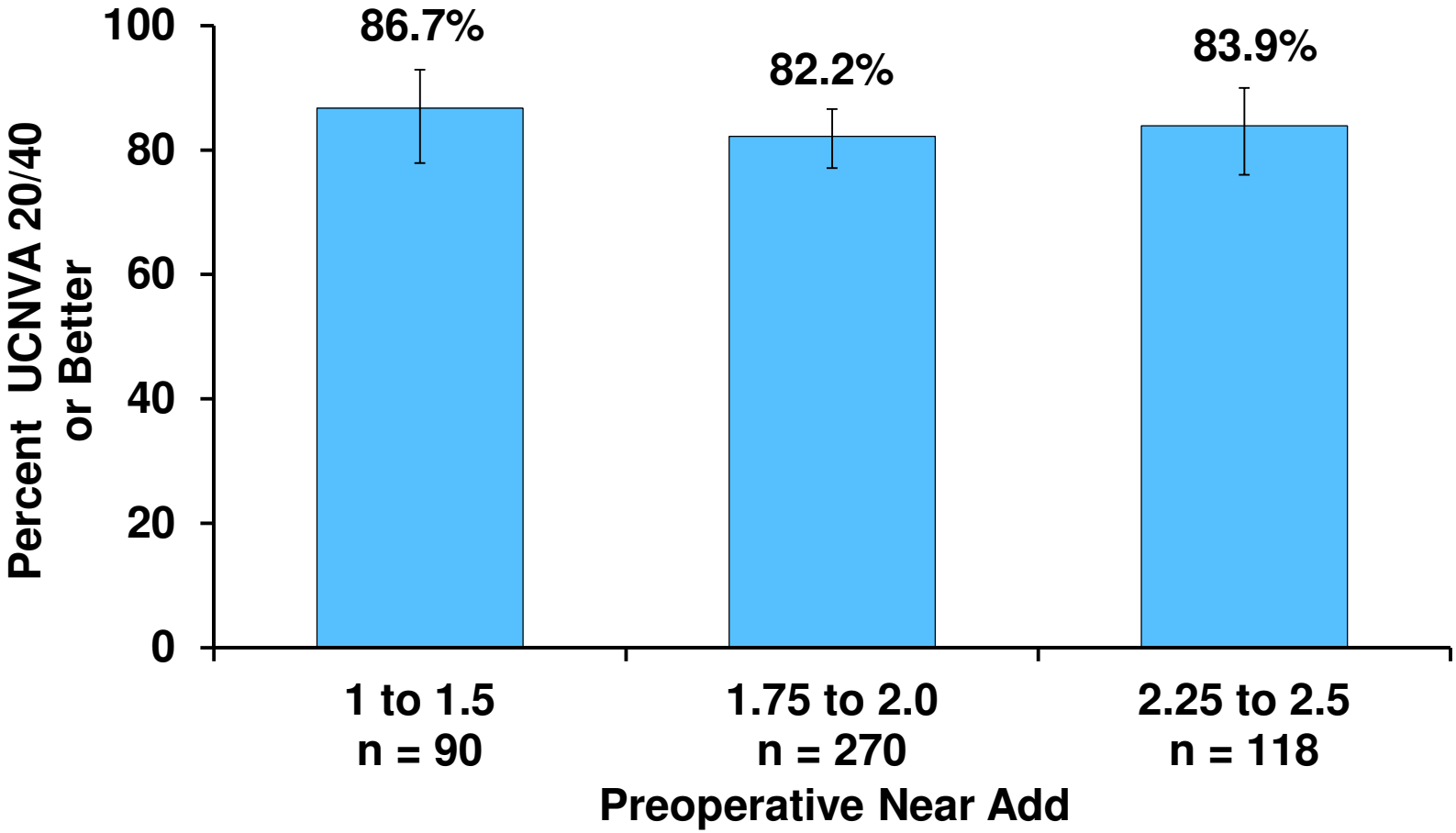


Pulfrich Effect: Results and Conclusions

	Simulated Inlay n = 6	KAMRA Inlay n = 6
Mean Neutralizing NDF value	0.275 ± 0.059	0.155 ± 0.132
Pulfrich Effect Seen	5	0
Pulfrich Effect NOT Seen	1	6
Total Subjects	6	6

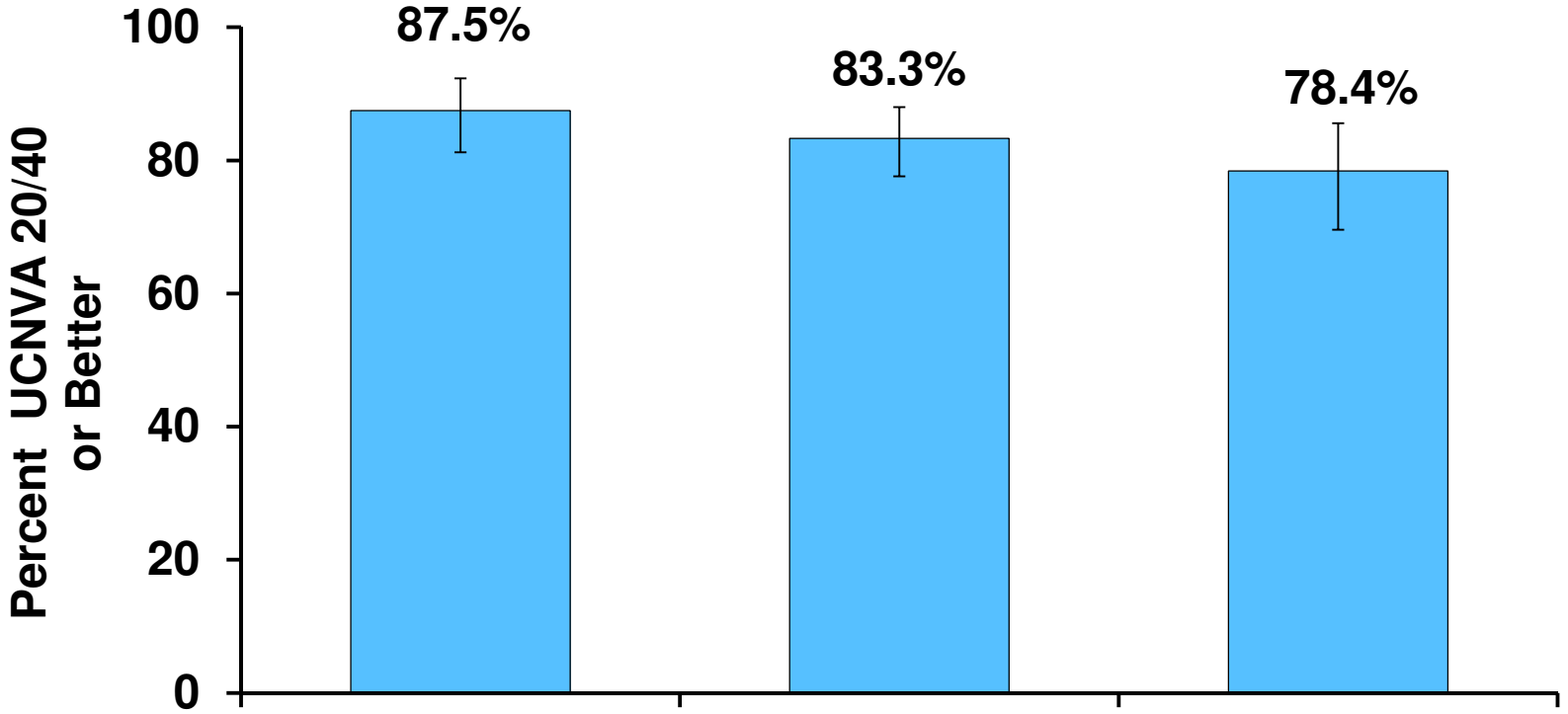
- Statistically significant Pulfrich effect seen in 5 of 6 simulated inlay subjects ($p<0.05$), vs. 0 of 6 in any KAMRA subjects
- Simulated inlay group more likely to observe effect over KAMRA group ($p=0.007$)
- Results of KAMRA subjects, with exposure times ranging 2-7 years, consistent with he hypothesis of adaption over time to the lower retinal illuminance in one eye, as well as with published reports of exposure to NDF in one eye for a few days caused a dampening over time of the initial Pulfrich effect

Primary Effectiveness Endpoint at 12 Months Stratified by Preoperative Near Add



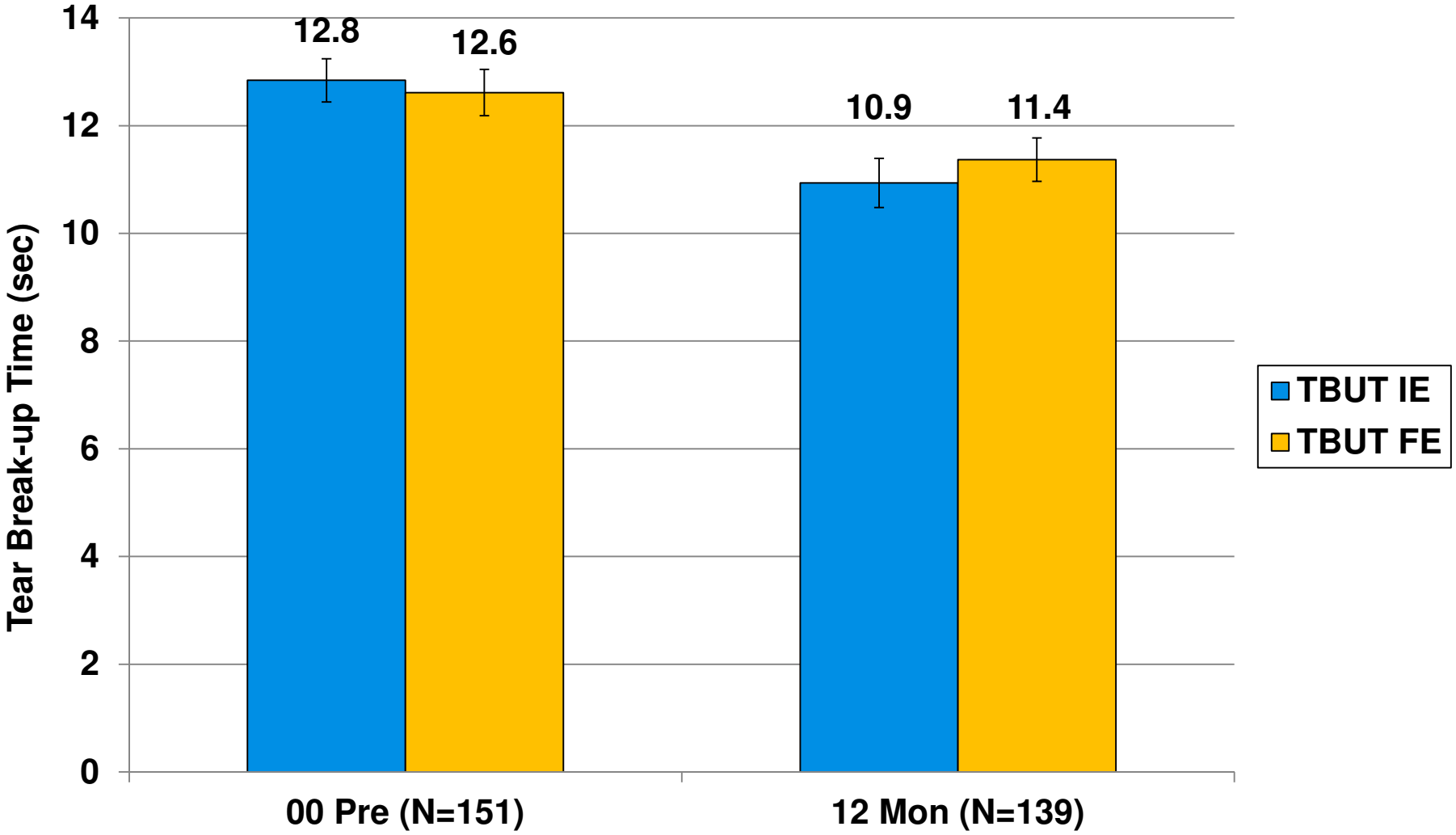
Mean UCNVA (SD):	42.3 (7.7)	40.7 (8.8)	39.7 (7.2)
Lines Improved (SD):	+3.0 (1.6)	+3.0 (1.7)	+2.8 (1.5)

Primary Effectiveness Endpoint 12 Months Stratified by Age



	45 to 49 n = 152	50 to 54 n = 215	55 to 60 n = 111
Mean UCNVA (SD):	42.2 (8.3)	41.1 (8.1)	38.1 (7.9)
Lines Improved (SD):	+3.1 (1.6)	+3.1 (1.6)	+2.8 (1.5)

Tear Break-up Time – Confirmatory Study



Cumulative Ocular AEs on All Removals: Post-removal Period (N=44)

Adverse Event	Number of Events	Number of Subjects	Comments
Corneal Edema with grade of ≥ 2+ (at one month or later)	3	2	occurred at post-removal 1 wk, 1 mo, 6 mo (Removed at 18-24, 30-36 mo, respectively)
Haze - Onset beyond 6 months with loss of BCDVA of ≥ 2 lines	1	1	occurred at post-removal 6 mo (Removed at 30-36 mo)
Decrease in BCDVA > 2 lines month 3 or later	3	3	occurred at post-removal 3 mo, 6 mo (Removed at 9-12, 12-18,12-18 mo, respectively)

All adverse events resolved within 3 months after onset

Change in MRSE from Baseline
All Available Eyes and Imputed